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META-ANALYSIS

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Meta-analysis on the association between the frequency of tooth brushing and hypertension risk

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Abstract

It is unclear whether the frequency of tooth brushing affects the risk of hypertension; thus, we conducted the first meta-analysis to focus on this topic. In this meta-analysis, we systematically searched the PubMed, Scopus, and Web of Science databases from their inception to October 2021 to identify eligible studies, while reference lists from retrieved review paper were also reviewed. We then conducted a meta-analysis of the highest compared with the lowest tooth brushing frequency, along with a dose-response meta-analysis, to explore this association. Subgroup and sensitivity analyses were conducted to identify the sources of heterogeneity. Publication bias was evaluated using Begg's and Egger's tests. We found eight relevant studies, three cohort and five cross-sectional, involving a total of 274 124 patients. Compared to the highest tooth brushing frequency, the lowest increased the risk of hypertension by 84.0% (OR 1.84; 95% CI, 1.44–2.35). Furthermore, a nonlinear dose-response relationship was observed ($P < .05$). The exclusion of any studies did not significantly alter the combined risk estimate, and no publication bias was detected. In conclusions, we report that epidemiological evidence supports the hypothesis that a lower frequency of tooth brushing is significantly associated with a higher risk of hypertension. Preventive interventions, such as adopting a good oral health routine, should be encouraged to maintain good general health.

KEYWORDS
hypertension, meta-analysis, tooth brushing

1 | INTRODUCTION

Hypertension is highly prevalent and causes 7.7 million premature deaths each year.[1] Moreover, it is a major risk factor for cardiovascular diseases, such as coronary heart disease, chronic kidney disease, and stroke, and places a significant burden on healthcare systems.[2–9] Given the adverse consequences of hypertension, identifying the associated factors and preventive measures are topics of key interest in public health. Several lifestyle factors have been linked to hypertension, including a high-salt diet,[10–12] insufficient exercising,[13–15] alcohol consumption,[16–19] and smoking.[20,21]

Tooth brushing is an important part of a healthy lifestyle and is considered a basic self-care behavior to maintain oral health.[22] Epidemiological studies have shown that poor tooth brushing habits

are associated with a series of health problems, including gingivitis, tooth decay,[23] periodontal disease,[24,25] head and neck cancer,[26] dyslipidemia,[27] and endothelial dysfunction.[28]

In addition, several epidemiological studies have shown that periodontal diseases are associated with hypertension.[29,30] Tooth brushing affects oral bacteria. Abnormal oral bacteria can induce periodontal diseases. More importantly, the spread of these through the body has been associated with several systemic diseases, including hypertension. Moreover, the gut is affected by oral bacteria. Animal and human studies have indicated that oral bacteria can translocate to the gut, changing its microbiota and potentially altering immune defenses.[31] Ectopic displacement of oral bacteria occurs in severe systemic diseases as well as in patients with chronic periodontitis. For example, Porphyromonas gingivalis causes dysbiosis in the subgingival microbiota and immune defense and may also cause gut dysbiosis.[31] Additionally, periodontal disease triggers inflammatory and immunological responses as well as the generation of inflammatory cytokines such as interleukin-6 (IL-6), leading to endothelial dysfunction and insulin resistance, all of which are risk factors for hypertension.[32]

As there are sufficient studies to summarize the evidence, the aim of this review was to investigate the association between tooth brushing and the risk of hypertension and to quantify the dose-response relationship between them.

2 | METHOD

2.1 | Literature search

We systematically searched the PubMed, Scopus, and Web of Science databases from the beginning to October 2021 to identify eligible original studies. The search strategy included "tooth brushing" OR "oral hygiene" OR "oral health" AND "cardiovascular" OR "hypertension." In addition, reference lists of the retrieved publications were searched to identify other relevant review papers.

2.2 | Selection criteria

Two authors (M.Y.Z. and L.Z.) independently assessed the identified publications for their relevance. Any disagreements were resolved through discussion with a third author (Z.X.L.). Studies meeting all of the following criteria were included in this review: (1) the study design was cohort, case-control, or cross-sectional; (2) the review paper was published in English; (3) tooth brushing was an exposure variable, and the outcome was hypertension; and (4) the study provided odds ratios (ORs) or relative risks (RRs) with 95% confidence intervals (CIs) or provided sufficient data to calculate them. Letters, reviews, clinical trials, animal studies, commentaries, and editorials were excluded.

Hypertension was defined as systolic and/or diastolic BP ≥ 140/90 mm Hg[33] or use of antihypertensive drugs at the time of interview.[34]

2.3 | Data extraction

Using a predefined form, two authors (M.Y.Z. and L.Z.) independently extracted the following information from the included studies: first author, year of publication, country of publication, study design, sex, age, number of participants, adjusted OR/RR with 95% CI, and adjusted factors. Disagreements between the two authors regarding the data extraction process were resolved by discussion.

2.4 | Assessment of study and evidence quality

The National Institutes of Health's Quality Assessment Tool for Observational Cohort and Cross–Sectional Studies was used to evaluate the quality of the studies.[35] This tool included 14 questions, and each "yes" answer scored one point. Each question had three response options: "yes," "no," and "other." "Other" had three meanings: "cannot determine," "not applicable," or "not reported." Each study was independently rated by two authors (M.Y.Z. and L.Z.). Discrepancies were resolved through discussion with a third investigator (Z.X.L.).

2.5 | Statistical analysis

The OR was considered the effect size of the relationship between tooth brushing and hypertension. A random-effects model was used to calculate the pooled OR and the I^2 statistic was used to assess heterogeneity across studies. In addition, if the review papers included at least three quantitative categories of tooth brushing, they were included in the dose–response meta-analysis. The dose value for each tooth-brushing exposure group was assigned as suggested by Cao et al.[36] : the median or mean level of tooth brushing within each category was used as the corresponding dose value. When the median or mean frequency of tooth brushing was not available, the midpoint of the upper and lower boundaries was considered the dose for each category. If the highest category was open-ended, the midpoint of the category was set at 1.5 times that of the lower category. Restricted cubic splines with three knots at percentiles of 10, 50, and 90% of the distribution were used to evaluate a potential curve linear relationship between tooth brushing and the risk of hypertension.

Subgroup analysis, stratified by sex, adjustment of covariates, and study design, was performed to investigate possible sources of heterogeneity. The metaregression was used to examine between-subgroup heterogeneity. A sensitivity analysis was conducted to evaluate data stability. Begg's and Egger's tests were used to evaluate publication bias. All statistical analyses were performed using STATA Ver.12 (Stata

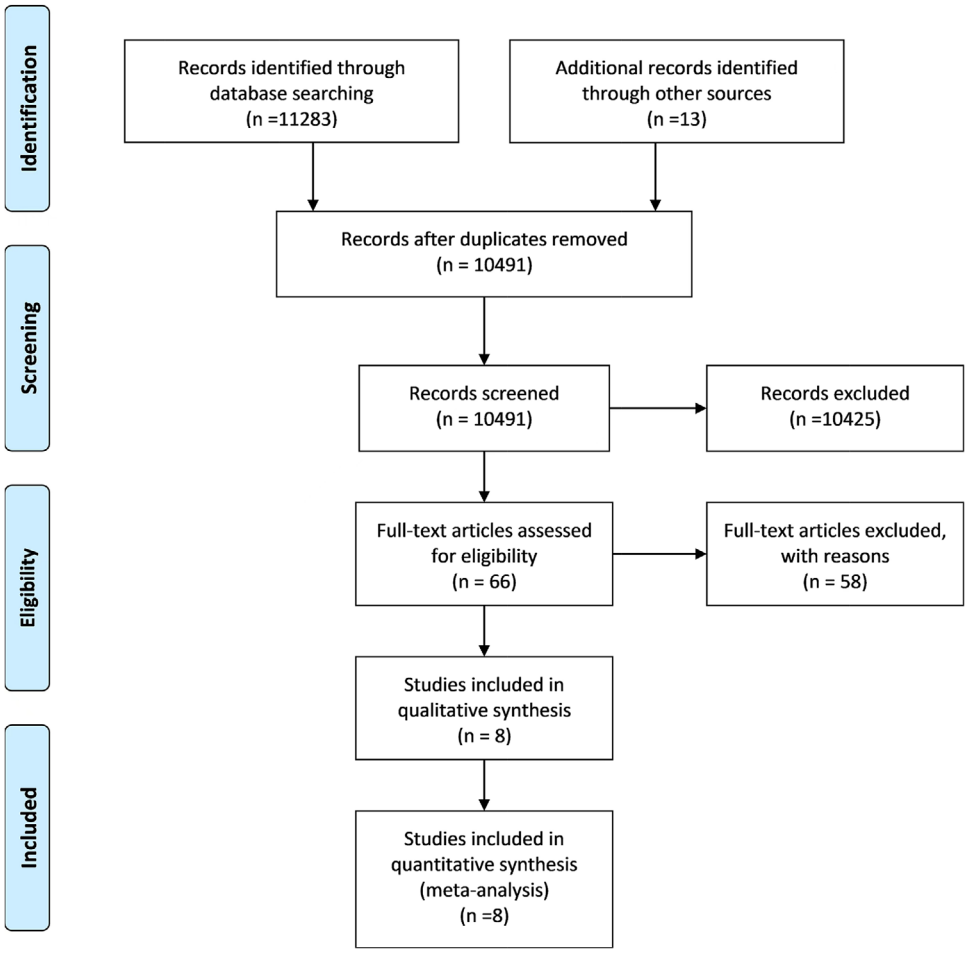

FIGURE 1 Flow-chart showing the process of study retrieval, selection and inclusion adopted in the present systematic review and meta-analysis

Corp, College Station, TX, USA). All tests were two-sided, and $P < .05$ was considered statistically significant.

3 | RESULTS

3.1 | Literature search

In total, 11 283 review papers were retrieved and reviewed (Figure 1). Following the inclusion of records identified through additional sources, and the removal of duplicates, 10 491 records remained. Then, titles and abstracts were screened, leaving 66 publications. Finally, eight studies[25,27,28,30,37–40] were included in this review: five cross-sectional and three cohort.

3.2 | Characteristics of included studies

Characteristics of eligible studies in the meta-analysis are shown in Table 1. The studies were published between 2009 and 2020 with a sample size ranging from 190 to 85 864. The quality scores of the eight studies were moderate or high (Table 2). The quality score for the five cross-sectional studies was 7.6 on average, ranging from 7 to 8. The quality scores of three cohort studies ranged from 7 to 9, with a mean of 8 points.

3.3 | Association between tooth brushing and the risk of hypertension

The results of the random-effects model combining the ORs for hypertension in relation to tooth brushing are shown in Figure 2. In total, eight studies investigated the relationship between tooth brushing and the risk of hypertension. The pooled OR of hypertension for tooth brushing was 1.84 (95% CI: 1.44–2.35), with substantial heterogeneity across studies ($P = .000$, $I^2 = 96.1\%$).

3.4 | Dose–response analysis

Five studies were included in the dose–response analysis of tooth brushing and the risk of hypertension. A nonlinear dose-response

TABLE 1 Characteristics of included studies

Study ID	Author	Year	Study Size	Country	Gender	Mean Age (SD)	Study design	Adjustment of covariates
1	Kajikawa	2014	190	Japan	M&F	57±18	Cross-sectional	None
2	Choi	2015	19560	Korea	M&F	19-95	Cross-sectional	Adjusted for age, sex, total body fat percentage, smoking, drinking, exercise, education, income, total energy intake, fat intake, and periodontitis.
3	Kuwabara	2016	85864	Japan	M&F	47±11.5	Cross-sectional	Adjusted for age, gender, body mass index, hypertension, diabetes mellitus, dyslipidemia, hyperuricemia and chronic kidney disease, and also for lifestyle habits—smoking, drinking, walk time and sleep time.
4	Matsui	2017	896	Japan	M&F	61	Cohort	None
5	Kuwabara	2017	10471	Japan	M&F	30–85	Cohort	None
6	Hwang	2018	8370	Korea	M&F	>30	Cross-sectional	Adjusted for age, gender, and significant covariates (P <.05)
7	Fujita	2009	76552	Japan	M&F	40–79	Cross-sectional	None
8	Daiki	2020	72221	Japan	M&F	45.6 (12.2)	Cohort	None

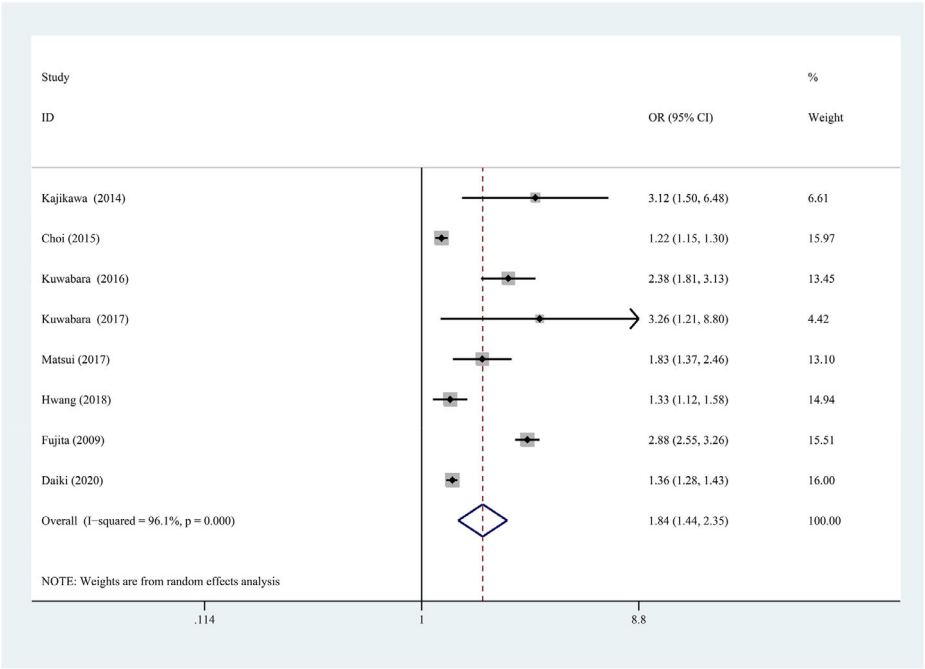

FIGURE 2 Association between tooth brushing and the risk of hypertension in a meta-analysis of observational studies. CI, confidence interval

association between the frequency of tooth brushing and the risk of hypertension was observed ($P < .05$), with substantial heterogeneity among studies ($P = .000$, $I^2 = 80.4\%$) (Figure 3). Pooling these studies, the risk of hypertension decreased by 22% for an increment of one tooth brushing per day (OR 1.22, 95% CI 1.01-–1.42).

3.5 | Results of subgroup and sensitivity analyses

To estimate differences by study characteristics level, subgroup analysis and metaregression were used, including the definition of sex, study design, sample size, controlling of covariates (yes and no). The

TABLE 2 Results of quality assessment

Criteria	Study ID							
	1	2	3	4	5	6	7	8
1. Was the research question or objective in this paper clearly stated?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Was the study population clearly specified and defined?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
3. Was the participation rate of eligible persons at least 50%?	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes
4. Were all the patients selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
5. Was a sample size justification, power description, or variance and effect estimates provided?	No	No	No	No	No	No	No	No
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	Yes	No	Yes	Yes	Yes	Yes	No	Yes
7. Was the time frame sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	No	No	No	No	No	No	No	No
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (eg, categories of exposure, or exposure measured as continuous variable)?	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
10. Was the exposure(s) assessed more than once over time?	No	No	No	No	No	No	No	No
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
12. Were the outcome assessors blinded to the exposure status of participants?	No	No	No	No	No	No	No	Yes
13. Was loss to follow-up after baseline 20% or less?	No	No	No	No	No	No	No	No
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?	No	Yes	Yes	No	No	Yes	No	No
Total score	8	8	9	7	8	8	7	9

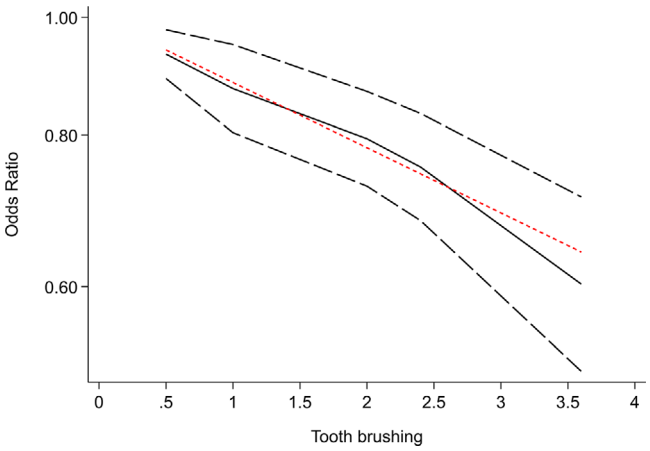

FIGURE 3 Forest plot of the summary odds ratio hypertension for a decrement of one time of tooth brushing per day

association between tooth brushing and hypertension was observed among almost all the subgroups; however, there were no significant between-group differences were observed for the above-mentioned factors (Table 3).

To identify the potential influence of a single study on the pooled results, any single study was excluded in turn and the results of the remaining included studies were pooled. The pooled OR did not change significantly, with a range from 1.41 (95% CI 1.24−-1.59) to 1.99 (95% CI 1.47−-2.53).

3.6 | Publication bias

Visual inspection of the funnel plot indicated a substantial asymmetry (Figure 4). No significant evidence of publication bias was found in the studies, as identified by Begg's test (Egger, $P = .183$ and Begg, $P = .536$).

TABLE 3 Results of subgroup analyses about tooth brushing and the risk of hypertension

Subgroup	Number of studies	OR/RR	95% confidence intervals	I^2(%)	P for heterogeneity	P for meta-regression
Sex						0.235
Male	2	1.147	0.988	1.306	0	0.506
Female	1	2.259	1.656	2.862	NA	NA
Mixed	8	1.765	1.471	2.058	92.9	<.001
Study design						0.776
Cross-sectional	5	1.98	1.32	2.65	95.8	<.001
cohort	3	1.53	1.11	1.95	46.6	0.154
Adjustment of Covariates						0279
Yes	3	1.47	1.11	1.82	83.9	0.002
No	5	2.19	1.23	3.15	94.5	<.001
Sample size						0.933
<1000	2	2.14	1.33	3.44	42.7	0.186
1000–20000	3	1.29	1.10	1.52	55.9	0.103
20000–100000	3	1.84	1.44	2.35	96.1	<.001

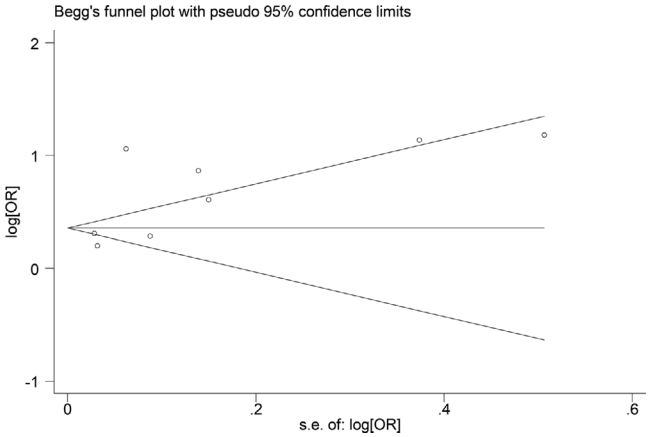

FIGURE 4 Funnel plot with 95% confidence interval

4 | DISCUSSION

Tooth brushing is a widespread oral care practice, and previous studies have suggested that tooth brushing may affect overall health. In our meta-analysis, we found that lower frequencies of tooth brushing were significantly associated with a higher risk of hypertension, which is in line with findings from a mechanism study.[29] Current evidence suggests that tooth brushing is an effective way to remove plaque[23] and reduces the risk of periodontal disease.[41] Inflammation caused the periodontal tissue to become a periodontal environment, and a large amount of local proinflammatory factors were released into the blood circulation, affecting the sympathetic nerves, and the renin-angiotensin-aldosterone system, which caused blood pressure to rise.[42–45] Besides, low frequency of tooth brushing activity contributes to the proliferation of Porphyromonas gingivalis, and these bacteria would worsen the enteric environment, finally leading to periodontal inflammation and abnormal immune responses.[27,42] Moreover, periodontal disease activates the immune system either directly or through its effect on the gut microbiome, which ultimately produces chronic inflammation-induced hypertension.[31] T cells are central to the immune response that contributes to hypertension.[47] They are activated in part by binding to specific antigens that are present in major histocompatibility complex molecules on professional antigen-presenting cells, and they generate repertoires of rearranged T-cell receptors. Activated T cells infiltrate tissues and produce cytokines, including interleukin 17A,[48] which promotes renal and vascular dysfunction and end-organ damage leading to hypertension.[49] Periodontitis and inflammatory bowel disease (IBD) share common dysbiotic and immunological features.[50] Thus, periodontitis can activate the chronic inflammatory state associated with autoimmunity. Prevalent hypertension in autoimmune disease with the impact of immune system dysfunction on vascular dysfunction and renal hemodynamics as primary mediators, with oxidative stress as the main contributor.[49]

This study highlights the need for further investigation into the relationship between tooth brushing, periodontal disease, and hypertension, in order to prevent the occurrence of periodontal disease, hypertension, and resulting organ damage through improved oral hygiene. This relationship could be explained by bacteremia or endotoxemia originating from periodontal pockets that lead to the systemic diffusion of inflammatory mediators from the lesion.[31–47] Alternatively, there could be an impairment of gut barrier function and modulation of the gut immune profile, induced by dysbiotic oral bacteria-mediated gut dysbiosis, as a result of endotoxemia and systemic inflammation.[31] Therefore, whether it is a direct or indirect pathway, we can determine the relationship between periodontal brushing-disease and hypertension. Interest has increased in the association between tooth brushing

and the risk of hypertension among the general public. Although the potential mechanisms by which less frequent tooth brushing increases the risk of hypertension have not been studied thoroughly, our meta-analysis of eight studies involving 274 124 patients showed an association between the two. Evidence from these studies suggests that individuals who brushed teeth with the lowest frequency had an increased risk of hypertension by 84% compared with those who brushed teeth with the highest frequency. We also found relatively high heterogeneity among the included studies on the association between the frequency of tooth brushing and the risk of hypertension.

To explore the source of heterogeneity, we conducted subgroup analysis, and the results showed that relatively high heterogeneity was found in undifferentiated sex, cross-sectional studies, and unadjusted confounders. Therefore, we assumed that the high heterogeneity in our meta-analysis might be due to these factors. Furthermore, we conducted a metaregression in our revised manuscript, and the results showed that there were no significant between-group differences in the above-mentioned subgroup. Therefore, further cohort studies are needed to investigate the association between tooth brushing and hypertension and focusing on distinguishing sex and adjusting for confounding factors.

Besides, our meta-analysis was limited to original research studies, and the populations in these were not well distributed. Furthermore, the original studies included in this meta-analysis are also not well distributed in terms of participant geography and age, as they primarily represent Asia and the middle-aged to elderly populations. Therefore, future studies on the association between the frequency of tooth brushing and the risk of hypertension should cover a wider, more representative population. Additionally, antiseptic mouthwash was an important confounding factor. However, our meta-analysis was constrained by the original studies, and these did not contain the confounding factor of antiseptic mouthwash; therefore, our meta-analysis excluded a discussion of confounding factors such as antiseptic mouthwash. Considering that the inclusion of confounding factors in the original studies could affect the validity of the meta-analysis's combined effect value, we conducted a subgroup analysis after adjusting for confounding factors, and the results of the two groups were relatively consistent. In addition, as living standards and incomes increase, more people are using antiseptic mouthwashes. Therefore, it is suggested that antiseptic mouthwash be included as a confounding factor in future original research on the frequency of tooth brushing and hypertension risk.

However, the frequency of tooth brushing varies based on the habits of individuals. Oral medical and dental workers suggest that brushing teeth twice per day, especially before going to sleep, has a significant effect on maintaining a good oral health status.[41,51] Food debris and bacteria accumulated during the day harm oral health and often lead to periodontal diseases followed by a series of adverse reactions. Brushing before going to bed is more important because it can remove food residue and dirt from daily meals. Moreover, oral saliva secreted at night can reduce the ability to resist bacteria, which is likely to lead to tooth decay and periodontal diseases. In addition, the mouth is closed at night, and the food is processed by glycolysis under hypoxic conditions, which provides a good breeding condition for anaerobic bacteria. Dental healthcare professionals should educate their patients on the importance of twice-daily tooth brushing. Teachers, especially those working in rural kindergartens and primary schools, should also educate young students to cultivate good habits of regular tooth brushing.

Additionally, Physical inactivity and smoking have been recognized as risk factors for hypertension, but our meta-analysis and a growing number of studies have found that a low frequency of tooth brushing is associated with hypertension risk, and good oral hygiene can help prevent and control hypertension. Therefore, the relevant departments should incorporate a low frequency of tooth brushing into the risk factors of hypertension when formulating hypertension prevention policies in the future, publicize it among residents widely, and enhance public awareness to increase the frequency of tooth brushing and reduce the risk of hypertension. From an economical perspective, brushing teeth is the simplest and most sustainable oral health behavior. Therefore, regular targeted brushing education programs should be implemented.

Our study has several strengths. This is the first meta-analysis to estimate the strength of the association between tooth brushing and hypertension. Furthermore, the sensitivity analysis and consistent results from various subgroup analyses indicated that our findings were reliable and robust, although heterogeneity existed among the included studies. Our study has some limitations. First, we included only eight studies, which limited the statistical power of the analyses. Thus, every country should pay more attention to research on tooth brushing and hypertension. Second, not only the frequency but also the quality and quantity of tooth brushing may affect blood pressure. Evaluation of the effects of both the quality and quantity of tooth brushing on blood pressure would enable more specific conclusions to be drawn.

5 | CONCLUSIONS

In conclusions, our meta-analysis found that low frequency of tooth brushing was significantly associated with an increased risk of hypertension. Given the high economic cost of hypertension, the findings of our study provide additional valuable clues for the prevention of hypertension. Further prospective and interventional studies are required to investigate the underlying processes of the associations between tooth brushing and hypertension.

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CONFLICT OF INTEREST

We declare we have no conflict of interest. All the authors have read and approved the manuscript submitted.

AUTHOR CONTRIBUTIONS

Li Zou and Mingye Zhang; methodology, Li Zou, Mingye Zhang and Zuxun Lu; formal analysis, Li Zou, Wenning Fu, and Yifang Liu; Data curation, Mingye Zhang, Wenning Fu, and Yifang Liu; writing—original draft preparation, Wenning Fu; writing—review and editing, Li Zou, Mingye Zhang, and Zuxun Lu; visualization, Li Zou and Jing Wen; supervision, Zuxun Lu. All authors have read and agreed to the published version of the manuscript.

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