The Relationship Between Tooth Loss and Hypertension: a Systematic Review and Meta-analysis

Akio Tada (atada@hyogo-dai.ac.jp)
Hyogo University
Rumi Tano
National Institute of Public Health
Hiroko Miura
University of Hokkaido

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Abstract

Understanding association between tooth loss and hypertension is important for improving cardiovascular health. We searched for publications that were published between July 2011 and June 2021 using three electronic databases (PubMed, EMBASE, and Scopus) and conducted a systematic review and meta-analysis on the association between tooth loss and hypertension. Quality assessments were performed using the Critical Appraisal Skills Program guideline, Newcastle–Ottawa Scale and the GRADE approach. Twenty studies (17 cross-sectional studies, and 3 cohort studies) met the inclusion criteria for this review. Most cross-sectional studies showed that subjects with more tooth loss exhibited a greater proportion of hypertension and higher systolic blood pressure than those with less tooth loss. Meta-analyses revealed a statistically significant association between tooth loss and hypertension. The pooled ORFs of hypertension for having tooth loss with no tooth loss and for edentulous with dentate were 2.22 (95% CI 2.00-2.45) and 4.94 (95% CI: 4.04–6.05), respectively. In cohort studies, subjects with more tooth loss had a greater incidence of hypertension than those with less tooth loss during the follow-up period. The present systematic review and meta-analysis suggested that tooth loss is associated with an increased risk of hypertension and higher systolic blood pressure.

1. Introduction

1.1 Background

Hypertension is a medical condition in which blood pressure is chronically 140/90 mmHg or higher[1]. The worldwide prevalence of hypertension has increased two-fold from 1990 to 2019, with more than 30% for both men and women aged 30–79[2]. Although high blood pressure does not typically cause symptoms, long-term high blood pressure is a major risk factor for coronary artery disease, stroke, heart failure, atrial fibrillation, peripheral arterial disease, vision loss, chronic kidney disease, and dementia[3–6].

Risk factors for hypertension include obesity[7], excessive intake of salt[8,9], heavy alcohol consumption[10,11], insufficient physical activity[12,13], psycho-social stress[14,15] and smoking[16].

Several studies in dentistry have reported that patients with periodontitis have higher blood pressure[17–19]. An estimated mechanism for the association between periodontitis and hypertension is endothelial dysfunction elicited by periodontitis[20]. The balance between cardiac output and peripheral vascular resistance is important for the maintenance of a normal blood pressure. In most cases of essential hypertension, peripheral resistance occurs, but normal cardiac output does not. However, endothelial dysfunction causes increase of blood pressure due to increased peripheral vascular resistance by elevated contractility and impairment of relaxation ability of blood vessels

Periodontitis progression results in tooth loss and higher number of tooth loss leads to a decline in masticatory function. Decreased masticatory function is likely to elicit deterioration of diet, increased intake of fatty food, and subsequent obesity[21], which may have influence on the incidence of hypertension.

An increasing number of studies have addressed the association between hypertension and tooth loss. However, no study has systematically reviewed articles that analyzed the association between tooth loss and hypertension.

1.2 Objective

The aim of this study was to systematically review the relationship between tooth loss/ number of teeth and hypertension.

2. Material And Methods

This systematic review was structured following the PRISMA Checklist. A protocol to address the a priori research questions, comprehensive literature search with inclusion and exclusion criteria for studies, screening methods, data abstraction, scientific study quality, and data analysis was developed to minimize bias.

2.1. Literature Search

The PICO model[22] was used to select eligible studies in the present systematic review. The inclusion criteria were defined according to the population (P; “human adults”), intervention or exposure (I; “impact of tooth loss on hypertension”), comparison (C; “different number of remaining teeth, different number of missing teeth or dentate and edentulous”), and outcome (O; “hypertension”). The eligibility of the studies was assessed by three independent authors (Akio Tada, Rumi Tano and Hiroko Miura) by screening the titles and abstracts, according to the PICO model. The following PICO question was used: “Does tooth loss/ number of teeth associate with hypertension?”. The inclusion criteria were defined as followed: (1) written in English, (2) published between 2011 and 2021, (3) investigating the association between tooth loss/number of teeth and hypertension, (4) conducted on adult subjects (age ≥ 18 years), and (5) using quantitative methods of data collection, were included in this review. Epidemiological studies on adults were also included. The exclusion criteria were defined as followed: (1) not written in English, (2) subjects were those aged 17 yeas and younger, or received oral and maxillofacial surgery or radiotherapy, (39 descriptive studies, reviews or studies with no analyses investigating the association between tooth loss and hypertension.

A literature search was performed in the following databases: PubMed, EMBASE, and Scopus databases with relevant keywords (Mesh and non-Mesh) as below ((“tooth loss” OR “number of teeth” AND “hypertension”) and (“tooth loss” OR “number of teeth” AND “blood pressure”).

2.2. Quality Assessments

The studies that met the inclusion criteria were appraised for quality using the Critical Appraisal Skills Programme (CASP) [23]. The checklist for the cohort studies was partially modified for application to cross-sectional studies (e.g., questions concerning the follow-up of participants were excluded). Each question was scored based on a response of “yes,” “no” or “cannot tell”; a response of “yes” was given a score of 1. Three independent authors (Akio Tada, Rumi Tano and Hiroko Miura) calculated the strengths and weaknesses of each study using the CASP checklist items, and assigned them a grade of “high,” “moderate,” or “low”. Both review authors agreed on the quality rating for each included study.

2.3. Assessment of risk of bias in the included studies

For each selected observational study, the risk of bias was evaluated according to the criteria described by the Newcastle–Ottawa Scale (NOS) for cohort studies. This scale encompasses three domains: selection (four items), comparability (one item), and outcome (three items)[24]. Cross-sectional studies were graded as follows: very good,

9–10; good, 7–8; satisfactory, 5–6; unsatisfactory, 0–4[25]. Cohort studies were graded as follows: very good, 8–9; good, 7; satisfactory, 5–6; unsatisfactory, 0–4[26].

The overall quality of evidence was evaluated using the Grading of Recommendation, Assessment, Development and Evaluation (GRADE) framework[27]. In this review, a narrative GRADE was chosen according to the types of studies included. The certainty of the evidence was evaluated for the study design, risk of bias, inconsistency, indirectness, and imprecision parameters, with categorization into one of four ratings: —high, moderate, low, and very low[28]. Evidence issued in this review includes observational data, it started at low quality and then other issues within the magnitude of the effect, inconsistency, indirectness, imprecision, and counteracting plausible residual bias or confounding could be used to downgrade the evidence[29]. However, the quality of evidence can increase when studies strictly meet one of the following criteria: the magnitude of the treatment effect is very large, there is evidence of a dose–response relationship, or all plausible biases would decrease the magnitude of the treatment effect[30].

2.4. Data extraction

Data were extracted from each eligible study by two independent authors (AT and HM) using a specifically developed data extraction sheet. Disagreements were resolved by consensus. The following data extracted from each study that were rated as eligible included first author, publication year, setting, type of study, number of subjects, confounding factors, and main findings including both adjusted odds ratios and 95% confidence intervals (CIs).

2.5. Statistical analysis

Meta-analyses were conducted using a random-effects model. Studies were excluded if they did not report an outcome in each group or did not have enough information available to calculate the OR. The numbers of subjects according to the status of the remaining teeth and the presence of hypertension were extracted from each study. A separate meta-analysis was performed for each outcome variable. Effect sizes were reported as pooled odds ratios with 95% confidence intervals (CIs) for categorical outcomes. The heterogeneity of the effect size estimates across these studies was quantified using the I^2 statistic. The I^2 statistic ranges from 0 to 100% ($I^2 < 25\%$, low heterogeneity; $I^2 = 25\%$-50%, moderate heterogeneity; and $I^2 \geq 50\%$, substantial heterogeneity)[31]. All data analyses were performed using the STATA version 16.

3. Results

3.1. Literature searches and study characteristics

The initial comprehensive literature search identified a total of 332 articles, and eligible articles were retrieved through a manual search (Fig. 1). After the removal of duplicates, the titles and abstracts of 217 records were screened. Of these, 186 articles were excluded according to the exclusion criteria written in the “Material and Methods”. The remaining 31 articles were screened for further analyses as follows.

Of the 31 potentially relevant articles, 11 were excluded because they did not meet the inclusion criteria written in the “Materials and Methods”. Finally, a total of 20 publications (17 cross-sectional studies[32–48], and three cohort studies[49–51]) were included in this systematic review, as shown in the flow chart (Fig. 1).

Characteristics of studies are presented in Table 1. In terms of blood pressure, 16 studies[32–37, 41–47, 49–51] categorized blood pressure into hypertension and normal according to global criteria[52] and six studies used values of systolic blood pressure (SBP) and diastolic blood pressure (DBP) and did not categorized them into hypertension and normal. Four studies used self-reported information about whether participants had hypertension[35, 40, 41, 48].

In terms of the number of teeth, 10 studies evaluated the number of missing teeth[32–40, 51] and 10 studies evaluated the number of remaining teeth[41–50]. In the analyses, only four studies used measured values[34–36, 40] while the other 16 categorized measured values. Categorizations were vastly different.

Regarding the age range of subjects, 7 studies included patients < 40 years[32, 39–42, 45, 48]. Three studies used menopause women[34, 36, 49].

The distribution of countries where the included studies were conducted is as follows: Asia, 9; Central-South America, 5; North America, 4; and Europe 2.

3.2. Quality Evaluation for each article

Quality evaluation of the included studies was performed using CASP, and the results are presented in Table 2. For all the studies, there was a clear focus. Five of the studies (cross sectional) recruited subjects from a clinical setting[32, 35, 38, 42, 43], which has a higher risk of selection bias. Seven studies used self-reported information on the number of teeth and four studies used self-reported information for hypertension in their analyses, which lowed the rating. Seven studies did not adequately control their analyses for all the potential confounders, such as sociodemographic and, socio-economic factors, health habits and general health for hypertension [32, 35, 36, 38, 42, 43, 46]. The studies were rated as follows: three were rated “High” (all cross-sectional studies) [41, 45, 47]; 15 “Moderate” (13 cross-sectional studies, and two prospective cohort studies) [32–40, 43, 44, 46, 48, 49]; and two “Low” (one cross-sectional study, and one prospective cohort study) [52, 50].

The quality of the studies was also evaluated using NOS scores (Table 3). Four studies were classified as “very good” [34, 41, 45, 47], 11 as “good” [32,33, 37–40, 44, 46, 48, 49, 51], four as “satisfactory” [35, 36, 42, 40] and one as “unsatisfactory” [43].

3.3. Quality Evaluation for Evidence

The overall certainty of the two pieces of evidence was evaluated using the GRADE system. The certainty of evidences stayed in “Low”, initial rating of observational studies, with no upgrading and downgrading shown as shown in Table 4.

3.4. Association between number of remaining/missing teeth and hypertension

The prevalence of hypertension was compared between/among groups with different number of remaining teeth in seven cross sectional studies[41–47] (Table 1). Five of the seven studies showed negatively significant associations between the number of remaining teeth and hypertension after controlling confounders [41–44, 46]. In one study, a significant association disappeared after control for confounders[47]. Another study found that the association was slightly below the threshold of statistical significance[43], while a different study failed to find an association between the number of remaining teeth and hypertension[45].

Six cross-sectional studies analyzed the association between number of missing teeth and hypertension[32, 33, 34, 35–37] (Table 1). All the studies displayed that positively significant associations after adjusting with confounding factors. Two studies showed that group with hypertension had higher mean[36] or median[35] of number of missing teeth than normal blood pressure group. Another study showed that menopausal women with hypertension had a higher number of remaining teeth than those without hypertension[36].

3.5. Association between number of remaining/missing teeth and SBP/DBP

Two of the studies analyzed the associations between number of remaining and SBP/DBP[46, 47](Table 1). Of these, one study showed that the population with a higher number of remaining teeth exhibited a significantly higher SBP than the population with a lower number of remaining teeth, but this association was not observed with DBP[47]. However, the significance disappeared after adjusting for covariates. Another study demonstrated that the number of remaining teeth was inversely associated with SBP and DBP even after adjusting for covariates[46].

A further four studies analyzed the associations between number of missing teeth and SBP/DBP[38–40, 48](Table 1). Two studies reported that populations with a greater number of missing teeth exhibited significantly higher SBP than those with a smaller number of missing teeth [38, 39] but this significance disappeared after adjustment with potential confounding factors. Regarding DBP, no significant difference was found in either study. In Darnard's study[38], a sub-population with missing teeth > 10 was more likely to have SBP > 140mmHg by 1.17 times than the sub-population with missing teeth ≦ 10 among adults aged < 65 years. However, this association was not observed among adults aged ≥ 65 years. On the other hand, one study found that a population with more missing teeth had significantly higher SBP than the population with fewer missing teeth after adjusting the confounding factors[48]. One study showed that the number of missing teeth was positively and significantly associated with SBP and DBP in multivariable linear regression models[40].

3.6 Cohort study

Three studies performed cohort study[49–51] (Table 1). Two studies have compared incidence of hypertension in regard with different number of teeth[49–50]. One study made a comparison between subjects who are edentulous and those who are dentate[49]. Edentulous participants had a significantly higher risk of incidence of hypertension after adjusting for confounders. Another study analyzed the association between the number of teeth at baseline and the incidence of hypertension during follow-up and found no significant association after adjusting for confounders[50]. One study compared missing teeth between subjects who had hypertension and those who did not at baseline[51]. In univariate analysis, the hypertension group had a higher risk of incidence of tooth loss than the normal group. However, in the multivariable analysis, the opposite result was observed.

3.7 Meta-analysis

Separate meta-analyses regarding the risk of hypertension were carried out for "no tooth loss" versus "tooth loss" and for "dentate" versus "edentulim". Three studies found that those with tooth loss have a significantly higher prevalence of hypertension than those with no tooth loss[37, 41, 42]. Based on the data of the studies for "no tooth loss" versus "tooth loss", the pooled summary OR was 2.22 (95% CI: 2.00–2.45) in the random-effect model for the group with having tooth loss compared to the non-tooth loss group (Fig. 2). In other words, the tooth loss group was 2.22-fold more likely to be diagnosed with hypertension. As for "dentate" versus "edentulim", two studies found that edentulous subjects had a significantly higher prevalence of hypertension that dentate subjects[37, 41] and the pooled

summary OR was 4.94 (95% CI: 4.04–6.05) in the random-effect model for the group with having edentulous compared to the dentate group (Fig. 3). The findings were statistically significant ($p < 0.001$). However, the statistical heterogeneity was high across all studies (I^2 = 94.8% and 99.1%, respectively).

4. Discussion

This systematic review was aimed to analyze the association between tooth loss and hypertension by systematically summarizing the scientific evidence derived from clinical studies during the last decade. Twenty studies were included, with a total of 745,140 adults. To the best of our knowledge, this is the first systematic literature review to examine this association. The results of this review may help elucidate the influence of oral health on blood pressure.

Although the majority of included studies were conducted in Asia, while few studies from Europe were included, countries where the study was conducted were prevalent in a wide range of the world. In Asia, such countries are prevalent in many areas (East Asia 4, South and South East-South Asia 3, Middle East 2). Since hypertension and tooth loss are common all over the country, these diseases may be targets for study in many countries. Since hypertension and tooth loss are common all over the country, these diseases may be targets for study in many countries.

Most of the included studies have demonstrated an association between tooth loss and hypertension. Individuals who had greater tooth loss exhibited a higher prevalence of hypertension and higher blood pressure than those who had less tooth loss. However, only two studies reported no association between tooth loss and hypertension without adjusting for possible confounding factors. According to our literature review, tooth loss is thought to have a considerable association with hypertension. However, a few studies reported that the significant association disappeared after adjusting with possible confounding factors and the odds ratios for this association in most studies, which ranges between 1 and 2, are not very large. Therefore, the extent of the association between tooth loss and hypertension may not be so great.

There are two possible cascades related to the association between tooth loss and hypertension. One is that periodontitis, a major cause of tooth loss, has been reported to be associated with hypertension. It is speculated that periodontitis progresses and consequently tooth loss and hypertension develop. The mechanisms by which periodontitis elicits hypertension are complex and not fully elucidated. It is likely that the major mechanism by which increase of blood pressure occurs in patients with periodontitis is spread of inflammation and secondary damage to the vascular endothelium[53–56]. Periodontal tissue covers a wide area of the oral cavity. The influence of local inflammation of periodontitis occurred in a large extent of the oral cavity may significantly contribute to systemic inflammation mediated by C-reactive protein and main inflammatory cytokines such as tumor necrosis factor alpha, interleukin 1b and interleukin 6[57–58]. Increase of nitrate-reducing bacteria, which is observed in patients with periodontitis may induce a reduction of nitric oxide, which may consequently lead to an increase in blood pressure[59–61]. It was also reported that an intervention of non-surgical periodontal treatment lead to an improvement of hypertension, accompanied with an improvement of periodontal status[62]. Another reason is that tooth loss causes a decrease in masticatory function, thereby inducing obesity. There are two possible explanations for the association between mastication and obesity. One is that the eating habits of people with poor masticatory function, and decreased consumption of vegetables and fruits, and higher consumption of high energy food, tend to cause obesity compared to those with adequate mastication[63–66]. Another is that less chewing leads to a decrease

in diet-induced thermogenesis and inactivation of neuronal histamine, which may consequently leading to obesity[67–69].

In patients with metabolic syndrome, other factors, such as diabetes and hyperlipidemia, add to this complex relationship. Obesity is one of the causes of diabetes and diabetes and periodontitis have a bidirectional relationship. In some of the studies reviewed in this article, the association between tooth loss and hypertension disappeared after adjustment for confounders. This suggests that other factors do have a considerable influence on this association. It is thought that various factors interact with each other in a complicated cascade from tooth loss to hypertension.

A significant association between SBP and tooth loss was observed, although it disappeared after adjustment for confounders, in studies included, however, the association between DBP and tooth loss was not significant. The reasons why SBP exhibits a higher association with tooth loss than DBP is unclear. The proportion of individuals with diastolic hypertension (systolic–diastolic hypertension [SDH] or isolated diastolic hypertension [IDH]) decreased, while those with systolic hypertension increased with age. Accumulation of advanced glycation end products (AGE) with aging leads to increased arterial stiffness and contributes to the development of ISH[70, 71]. Excessive intake of animal-derived foods that are rich in AGE may increase the risk of hypertension and other chronic disease [72–75]. In general, individuals who suffer from decreased masticatory function due to tooth loss tend to eat foods that are high in fat[76–79]. Tooth loss may induce AGE accumulation, consequently contribution to increased SBP.

Two prospective cohort studies demonstrated that individuals with more tooth loss exhibited a higher incidence of hypertension than those with less tooth loss during the observation period[49, 50]. On the contrary, one study reported that subjects with hypertension experienced lower tooth loss than those without hypertension[51]. The association between tooth loss and hypertension may not be bidirectional. In other words, hypertension may not cause tooth loss.

Overall, the studies included in this review have a large number of subjects. Eight of 20 included studies have investigated large-scale community dwelling of > 1000 [33, 37, 41, 44, 46–48, 51], which enhances the credibility of the results of the studies. Several studies have investigated many specialized subjects, including patients from clinics or hospitals [32, 35], menopausal women [34, 40, 49], and male health care specialists[50]. Although it is problematic to apply the results of these studies to the general population, the large number of subjects in their studies increases the reliability of the study results.

Of the 20 included studies, 14 (70%) adjusted the association between blood pressure and tooth loss with all possible confounding factors (demographic factors, socio-economic factors, health behavior and general health). Of the remaining six studies, 4 studies lacked only one confounding factor in adjustment. The most important confounding factor was obesity, and almost all studies used obesity in the adjustment. These warrant the reliability of the evidence obtained in this review. However, three studies that investigated patients from university hospitals failed to adjust for socio-economic factors. The characteristics of these studies' settings might make it difficult to obtain data of socio-economic factors.

Eight studies employed self-reported data on the number of teeth and/or hypertension. Some studies have shown that the validity of self-reported number of tooth loss in high-income countries is strong[76, 77]. One study examined in health professionals in the US, expecting high validity against clinically measured results[50]. However, the validity of

the self-reported number of lost teeth has not been evaluated in lower and middle-income countries. Moreover, the validity of self-reported hypertension in developing countries is not high[78, 79]. Since most of the studies that employed self-reported data on the number of teeth and/or hypertension in this review were performed in developing countries, self-reported data may deviate from true values. Since subjective measurements have the possibility to give considerable optimistic results compared with practitioners' measurements[80], self-reported data may often be underestimated.

There are several limitations in this study. First, all studies included in this review were observational studies. Intervention studies are necessary to analyze the causal relationships. Although lost teeth cannot be regenerated, they can be restored by prosthetics. Provision of prosthetics can improve both masticatory function and diet. When decreased mastication elicits obesity and subsequently hypertension, restoration of mastication by the provision of prosthetics may improve increased blood hypertension. The number of teeth is just an anatomical indicator. There is an indicator that is the sum of the number of natural teeth and the number of lost teeth that are restored by prosthetics. It is of interest to investigate the association between the number of functional teeth and hypertension.

Second, the grouping of participants according to the number of teeth differed among the studies. Because of this problem, only small-scale meta-analyses were performed. Moreover, the only meta-analyses that were carried out were to compare the hypertension rate for tooth loss vs. no tooth loss and for dentate vs. edentate. Pooled odds ratio data based on a cut-off value for the number of teeth is valuable for estimating the association between the number of remaining teeth and hypertension. Moreover, it may be a rough indication for maintaining oral health to prevent hypertension.

The strength of our study is that it included many studies with a large number of subjects. The greater the sample size, the smaller the error, which makes the results more reliable.

5. Conclusion

In the present review, we provided an overview and appraisal of studies regarding the relationship between the number of teeth/tooth loss and hypertension. People with fewer remaining teeth or more tooth loss exhibited a higher incidence of hypertension. Those with more tooth loss had significantly higher SBP but not DBP than those with less tooth loss. Those with more tooth loss showed a higher incidence of hypertension than those with less tooth loss during the observation period.

Declarations

Authors' contributions

Authors AT, RT and HM contributed to the conception, design of the study, acquisition of data, interpretation of data, and manuscript revisions. AT contributed to the writing.

Conflicts of Interest

The authors declare no conflict of interest.

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Tables

Table 1 Summary of studies on the relationship between tooth loss/number of teeth and hypertension

(1) Cross-sectional study for the association between loss/number of teeth and hypertension

Reference	Study sample	tooth loss/ number of teeth	hypertension	Control of confounding factors[a]	Key results
Mendes *et al*. (2021)	10576 patients from university clinic (dental) aged 18 years and older (Portugal)	Missing teeth <10 10 ≤	Hypertension Category SBP, DBP Mean±SD	1, 3, 4	the presence of hypertension (odds ratio (OR) = 1.04, 95% CI: 1.03–1.05) and grade 3 hypertension (OR = 1.03, 95% CI: 1.02–1.05) were associated with the number of teeth lost
Da *et al*. (2019)	3677 community dwelling aged 50 years and older (China)	Tooth loss ≦3, 4-14, ≥15	Hypertension category	1, 2, 3, 4	After adjusting for covariates (socio-demographic characteristics, health behaviors and other chronic conditions), teeth lost (15 or more) was significantly associated with grade III hypertension, with OR = 1.55(95% CI 1.09-2.20).
Gordon *et al*. (2018)	1341 postmenopausal women (US)	No. of missing teeth	Systolic blood pressure (SBP) Diastolic blood pressure (DBP)	1, 2, 3,4	Univariate models showed significant associations between severe tooth loss and SBP and PP, but not with DBP. However, the significance was taken away in fully adjusted generalized linear models.

[a] The following variables were controlled for in the analyses or with separate results: 1, demographic factors; 2, socio-economic factors; 3, smoking/alcohol; 4, flossing/brushing; 5, diabetes, hypercholesterolemia, and obesity

Continued

Reference	Study sample	tooth loss/ number of teeth	hypertension	Control of confounding factors[a]	Key results
Delgado-Perez *et al.* (2018)	60 patients in a health center (Mexico)	Number of missing teeth	hypertension	1, 2,	Individuals with hypertension had higher risk of more missing teeth (incidence rate ratios [IRRs] = 2.63;95% CI = 1.77–3.90)
Al-Ahmad *et al.* (2018)	60 postmenopausal women (Malaysia)	Number of missing teeth	hypertension		Postmenopausal women with hypertension showed more significant tooth loss compared to those with normal tension.
Singh (2016)	1486 community dwellings aged 45 years and older (India)	No loss of teeth Loss of some natural teeth Edentulous	Hypertension category	1, 2, 3, 4	Individuals with partial tooth loss had 1.62 times higher odds of being hypertensive than those without any tooth loss after adjustment of confounders.
Darnaud *et al.* (2015)	102,330 individuals, who underwent medical and oral examinations (France)	Missing teeth 10≥, 10<	SBP, DBP	1, 3, 4	Subjects <65 years with missing teeth>10 showed higher hypertension rate than counterpart (OR=1.17 95%CI= 1.07-1.31)
Hosadurga *et al.* (2020)	270 outpatients aged 20-59 (Malaysia)	Edentulous Partial tooth loss	SBP DBP Mean±SD	1, 2, 3, 4	After adjusting for other covariates, there was no significant association between tooth loss and SBP and DBP.

[a] The following variables were controlled for in the analyses or with separate results: 1, demographic factors; 2, socio-economic factors; 3, smoking/alcohol; 4, diabetes, hypercholesterolemia, and obesity

Continued

Reference	Study sample	tooth loss/ number of teeth	hypertension	Control of confounding factors[a]	Key results
Moghadam *et al.* (2016)	700 community dwellings aged 35 years and older (Iran)	Number of tooth loss	SBP, DBP	1,2,3,4	The average values for systolic and diastolic blood pressure of edentulous participants were obtained 8.02 and 6.64 mmHg (95% CI) respectively, higher than those who had ≥10 teeth in both arches.
Shin (2018)	13651 commuity dwelling aged 19 years and older Data from the 2015 Korean National Health and Nutrition Examination Survey (South Korea)	0, 1-19, 20-27, 28	SBP, DBP Hypertension category	1,2,3,4	The fully adjusted odds ratios (AOR) of the number of teeth group for hypertension were as follows: AOR: 1.25, 95% CI: 1.11 to 1.43 for 20 to 27 teeth; AOR: 1.46, 95% CI: 1.22 to 1.76; 1 to 19 teeth; and AOR: 1.63, 95% CI: 1.22 to 2.18 for edentulism.
Dar-Odeh *et al.* (2019)	10576 female patients from university clinic (dental) aged 18 years and older (Saudi Arabia)	No missing teeth Having missing teeth	Hypertension category	1, 3, 4	the presence of hypertension (odds ratio (OR) = 1.04, 95% CI: 1.03–1.05) and grade 3 hypertension (OR = 1.03, 95% CI: 1.02–1.05) were associated with the number of teeth lost

[a] The following variables were controlled for in the analyses or with separate results: 1, demographic factors; 2, socio-economic factors; 3, smoking/alcohol; 4, diabetes, hypercholesterolemia, and obesity

Continued

Reference	Study sample	tooth loss/ number of teeth	hypertension	Control of confounding factors[a]	Key results
Islas-Granillo *et al.* (2011)	139 elderly who resided at long term facility or attended adult day center aged 60 years and older (Mexico)	Edentulism Having teeth	Hypertension	1	Being edentate has a higher risk of hypertension with approaching significance (p=0.067)
Kim SW *et al.* (2016)	8058 community dwellings aged 40 years and older Data from the 2012 Korean National Health and Nutrition Examination Survey (South Korea)	0-19, 20-27, 28	hypertension	1,2, 3, 4	Women with 0-19 remaining teeth had the highest prevalence of hypertension after adjusting covariates
Laguzzi *et al.* (2016)	341 community dwellings aged 15-24, 35-44, 65-74 years (Urugay)	Having 20 teeth, edentulism	Hypertension	1,2,3,4	No association between tooth loss and hypertension.
Zhu H *et al* (2015).	5511 community dwellings aged (US)	0, 1-20, 21-27, 28		1,2,3	The number of natural teeth was inversely associated with blood pressure (p < 0.01).

[a] The following variables were controlled for in the analyses or with separate results: 1, demographic factors; 2, socio-economic factors; 3, smoking/alcohol; 4, diabetes, hypercholesterolemia, and obesity

Continued

Reference	Study sample	tooth loss/ number of teeth	hypertension	Control of confounding factors[a]	Key results
Del Brutto *et al.* (2020)	1543 community dwelling aged 40 years and older (Ecuador)	≥10 remaining teeth(n= 1117) <10 remaining teeth (n = 426)	Systolic blood pressure (SBP) Diastolic blood pressure (DBP)	1, 2, 3, 4	Univariate models showed significant associations between severe tooth loss and SBP and PP, but not with DBP. However, the significance was taken away in fully adjusted generalized linear models.
Peres (2012)	1720 community dwelling aged 20-59 years (Brazil)	Number Edentulous <10 teeth at least in one arch ≥10 in both arches	SBP, DBP	1,2,3,4	Edentulous subject had a SBP 8.3 mmHg (95%CI 0.1;16.7) higher than those with more than 10 teeth in both arches after adjustment for potential confounders.

[a] The following variables were controlled for in the analyses or with separate results: 1, demographic factors; 2, socio-economic factors; 3, smoking/alcohol; 4, diabetes, hypercholesterolemia, and obesity

(2) Cohort study for the association between loss/number of teeth and hypertension

Reference	Study sample	tooth loss/ number of teeth	hypertension	Control of confounding factors[a]	Key results
Gordon JH (2019)	36,692 postmenopausal women (US)	Edentulism Dentate	hypertension	1, 2,3,4	Edentulism was significantly associated with incident hypertension in adjusted (HR (95% CI) = 1.21 (1.11–1.30)) models.
Rivas-Tumanyan S (2012)	31543 male health professionals aged 40-79 (US)	Number of teeth 0-10, 11-16, 17-24, 25-32 Tooth loss during follow-up	hypertension	1,2,3,4	Significant associations between number of teeth or tooth loss during follow-up and incidence of hypertension were not observed.
Kim YT, (2013)	514,866 community dwellings aged 40-79 (South Korean)	Tooth loss	hypertension	1,2,3,4,	Subjects with hypertension showed 0.97-0.94-fold increased risk of experiencing a loss of ≥4 and 2-3 teeth

[a] The following variables were controlled for in the analyses or with separate results: 1, demographic factors; 2, socio-economic factors; 3, smoking/alcohol; 4, diabetes, hypercholesterolemia, and obesity

Table 2 The results of the critical appraisal assessment

(1) Cross-sectional study

	1	2	3	4	5a	5b	6	7	8	Quality assessment
Mendes (2021)	✓	*X*	✓	✓	*X*	✓	✓	*X*	✓	*Moderate*
Da (2019)	✓	✓	*X*	✓	✓	✓	✓	✓	✓	*Moderate*
Gordon (2018)	✓	✓	✓	✓	✓	✓	✓	*X*	✓	*Moderate*
Delgado-Perez (2018)	✓	*X*	✓	✓	*X*	✓	✓	*X*	✓	*Moderate*
Al-Ahmad (2018)	✓	✓	✓	✓	*X*	*X*	✓	*X*	✓	*Moderate*
Singh (2016)	✓	✓	*X*	*X*	✓	✓	✓	✓	✓	*Moderate*
Darnaud (2015)	✓	*X*	✓	✓	*X*	✓	✓	*X*	✓	*Moderate*
Hosadurga (2020)	✓	✓	*X*	✓	✓	✓	✓	✓	✓	*Moderate*
Moghadam (2016)	✓	✓	*X*	✓	✓	✓	✓	✓	✓	*Moderate*
Shin (2018)	✓	✓	✓	✓	✓	✓	✓	✓	✓	*High*
Dar-Odeh (2019)	✓	*X*	✓	*X*	*X*	✓	✓	*X*	✓	*Low*
Islas-Granillo (2011)	✓	*X*	✓	*X*	*X*	✓	✓	✓	✓	*Moderate*
Kim S (2016)	✓	✓	✓	✓	✓	✓	✓	✓	✓	*Moderate*
Laguzzi (2016)	✓	✓	✓	✓	✓	✓	✓	✓	✓	*High*
Zhu (2015)	✓	✓	✓	✓	*X*	✓	✓	✓	✓	*Moderate*
Del Brutto (2020)	✓	✓	✓	✓	✓	✓	✓	✓	✓	*High*
Peres (2012)	✓	✓	*X*	✓	✓	✓	✓	✓	✓	*Moderate*

✓*, satisfied; X, not satisfied; N, not applicable*.

1 Did the study address a clearly focused issue?

2 Were the subjects recruited in an acceptable way?

3 Was the exposure accurately measured to minimise bias?

4 Was the outcome accurately measured to minimise bias?

5 (a) Have the authors identified all important confounding factors?

5 (b)Have they taken account of the confounding factors in the design and/or analysis?

6 Do you believe the results?

7 Can the results be applied to the local population?

8 Do the results of this study fit with other available evidence?

(2) Cohort study

	1	2	3	4	5a	5b	6a	6b	7	8	9	Quality assessment
Gordon (2019)	✓	✓	*X*	✓	✓	✓	✓	✓	✓	*X*	✓	Moderate
Rivas-Tumanyan (2012)	✓	*X*	*X*	*X*	✓	✓	✓	✓	✓	*X*	✓	*Low*
Kim YT (2013)	✓	*X*	✓	✓	✓	✓	✓	✓	✓	✓	✓	*Moderate*

✓, satisfied; X, not satisfied; N, not applicable.

1-5b: The same as cross-sectional study

6a. Was the follow up of subjects complete enough?

6b. Was the follow up of subjects long enough?

7. Do you believe the results?

8. Can the results be applied to the local population?

9. Do the results of this study fit with other available evidence?

Table 3 Newcastle-Ottawa Scale score of included studies

(1) Cross-sectional study

	Selection				comparability	outcome		score	Evaluation
	1	2	3	4		1	2		
Mendes (2021)		*		**	*	**	*	7	Good
Da (2019)	*	*		*	**	**	*	7	Good
Gordon (2018)	*	*		**	**	**	*	9	Very good
Delgado-Perez (2018)				**	*	*:	*	5	Satisfactory
Al-Ahmad (2018)	*			**		**	*	6	Satisfactory
Singh (2016)	*	*		*	**	*	*	7	Good
Darnaud (2015)		*		**	*	**	*	7	Good
Hosadurga (2020)	*	*		*	**	**	*	8	Good
Moghadam (2016)	*	*		*	**	*:	*	7	Good
Shin (2018)	*	*		**	**	**	*	9	Very good
Dar-Odeh (2019)		*		**	*	*	*	6	Satisfactory
Islas-Granillo (2011)				**		*	*	4	Unsatisfactory
Kim S (2016)	*	*		**	**	**	*	8	Good
Laguzzi (2016)	*	*		**	**	**	*	9	Very good
Zhu H (2015)	*	*		**	*	**	*	8	Good
Del Brutto (2020)	*	*		**	**	**	*	9	Very good
Peres (2012)	*	*		*	**	**	*	8	Good

(2) Cohort study

	Selection				comparability	outcome			score	Evaluation
	1	2	3	4		1	2	3		
Gordon (2019)	*	*		*	**	*	*		7	Good
Rivas-Tumanyan (2012)		*		*	**		*	*	6	Satisfactory
Kim YT (2013)	*	*	*		**	*	*		8	Good

Table 4 Summary of evidences according to GRADE approach

No of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other consideration	Certainty
Association between tooth loss and hypertension							
16	Observational studies	Not serious	Not serious	Not serious	Not serious		Low
Association between tooth loss and blood pressure							
6	Observational studies	Not serious	Not serious	Not serious	Not serious		Low

Figures

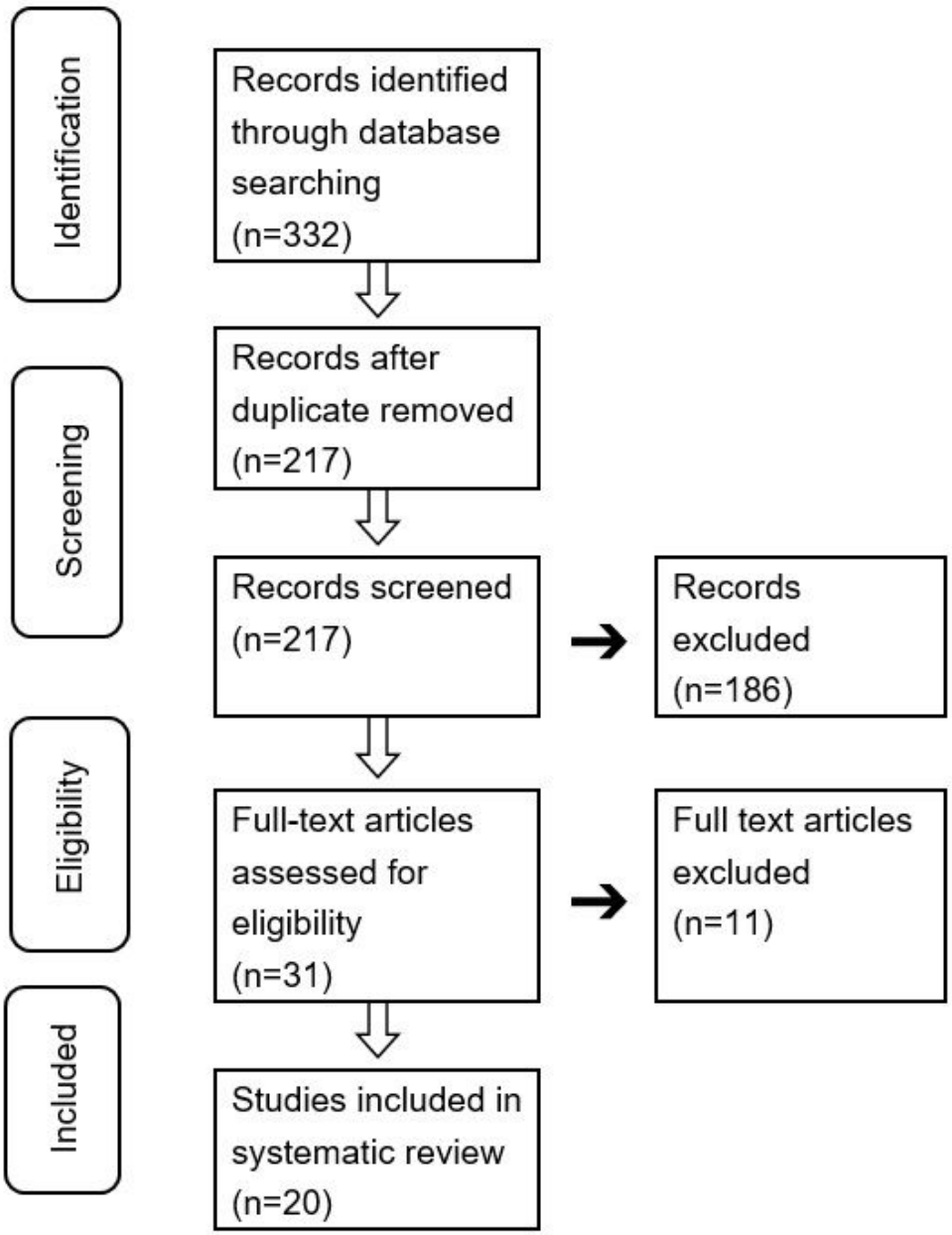

Figure 1

Flow diagram of literature search

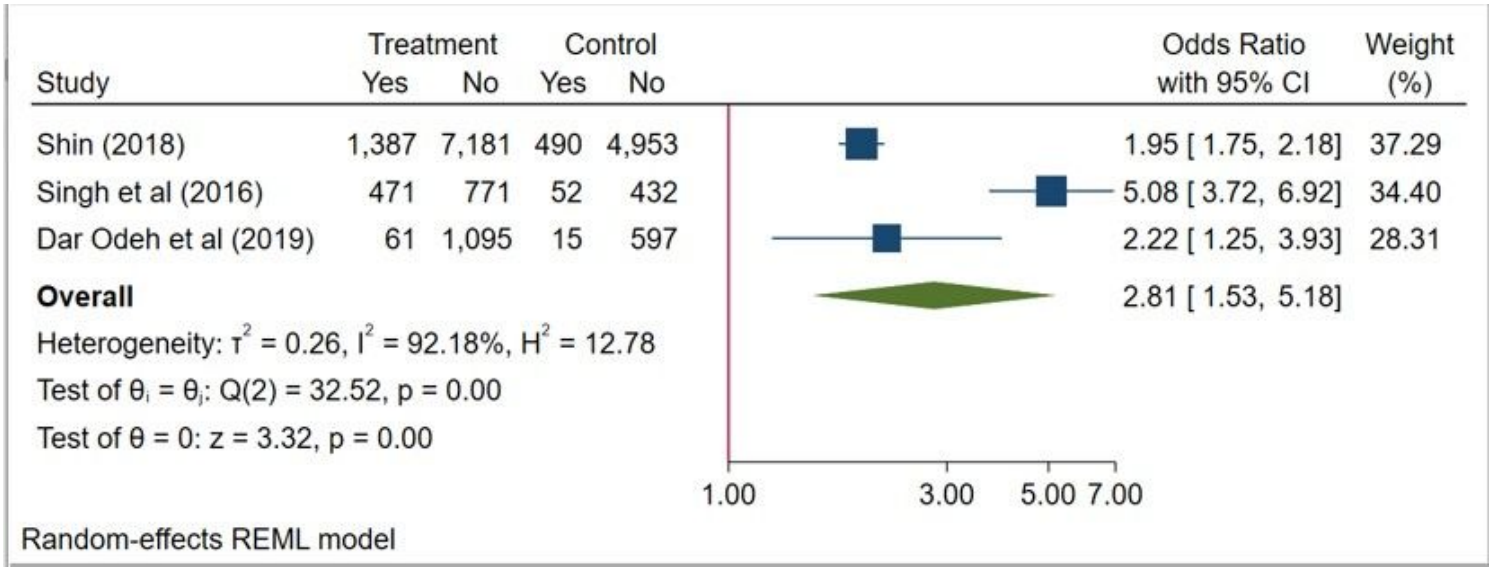

Figure 2

Forest plots of the Odds ratios with corresponding 95% Cis of studies on non-tooth loss/tooth loss and risk of hypertension

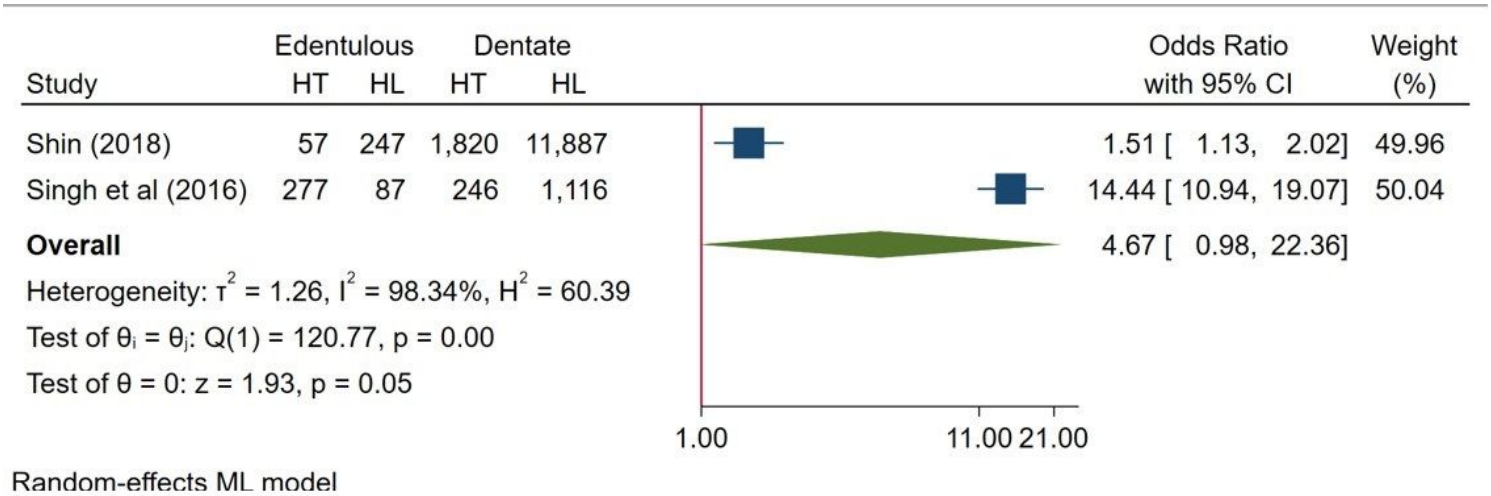

Figure 3

Forest plots of the Odds ratios with corresponding 95% Cis of studies on dentate/edentulous and risk of hypertension