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REVIEW ARTICLE

Prevalence of apical periodontitis and non-retention of root-filled teeth in hypertensive patients: Systematic review and meta-analysis

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Abstract

Background: Several studies have suggested a relationship between AP, as well as the loss of root-filled teeth (RFT), and hypertension (HTN).

Objectives: The aims of this systematic review and meta-analysis were to investigate the prevalence of AP, and non-retention of RFT, in hypertensive patients.

Methods: A search was performed in PubMed/MEDLINE, Web of Science, Scopus and EMBASE. The inclusion criteria established were studies published until February 2023, comparing hypertensive subjects with controls, assessing the prevalence of AP and/or providing data on the prevalence of non-retained RFT. Meta-analysis was performed using the RevMan (analyst) tool to determine the pooled prevalence of AP and loss of RFT. Risk of bias was assessed using the Cochrane Risk-of-Bias tool. The quality of evidence was assessed by GRADE.

Results: The search strategy identified 454 articles, and only eight met the inclusion criteria. Six studies had analysed the association between AP and HTN and two studies had analysed the association between non-retention of RFT and HTN. Meta-analysis showed and overall OR = 1.71 (95% CI = 0.92–3.16; $p = .09$) for the prevalence of AP among patients with HTN. The prevalence of non-retention of RFT among patients with HTN has an overall OR = 1.78 (95% CI = 1.60–1.98; $p = .000001$). The risk of bias in the individual studies was low or moderate, and the quality of the overall evidence has shown a level of certainty very low.

Discussion: There is no association between the prevalence of AP and HTN. In addition, hypertensive patients have significantly increased odds of losing RFT. Given the high prevalence of hypertension, it is very common to perform root canal treatments on hypertensive patients. It is imperative to communicate this heightened risk to patients and recommend periodic monitoring of oral health and hypertension, paying special attention to this subset of patients.

Registration: PROSPERO CRD42022302385.

KEYWORDS
apical periodontitis, endodontic medicine, hypertension, root canal treatment

INTRODUCTION

Hypertension (HTN) is a chronic medical condition in which the blood pressure (BP) in the arteries is elevated. The prevalence of high blood pressure is 30–45% in adult subjects with an acute increase with age (Piepoli et al., 2016). It can be primary or essential (90–95% of cases), which refers to high BP for which no medical cause can be found, or secondary (5%–10% of cases), caused by other conditions that affect the kidneys, arteries, heart, or endocrine system (Carretero & Oparil, 2000). HTN is diagnosed when the average of 2 or more diastolic BP measurements on at least 2 subsequent visits is ≥90 mm Hg or when the average of multiple systolic BP readings on 2 or more subsequent visits is consistently ≥140 mm Hg (Whitworth, 2003). Persistent HTN is one of the risk factors for stroke, heart attacks, heart failure and arterial aneurysm and is a leading cause of chronic kidney failure (Bakris et al., 2023).

HTN has been associated with dental problems, difficulties in bone healing after tooth extractions and implant loss as a result of defects in the process of osseointegration (Leite et al., 2005; Manrique et al., 2012).

Apical periodontitis (AP), an acute or chronic inflammatory process that involves the periapical portion of a tooth root, is principally caused by a bacterial infection that persists in the pulp space of tooth resulting in destruction of periradicular tissue (Siqueira & Rôças, 2008). The infectious aetiology of AP and the fundamental role of microbial factors induction, evolution and endurance have been extensively researched (Siqueira & Rôças, 2014). Radiographically, chronic AP can be observed as a radiolucent area around the root apex (López-López et al., 2015). It is a notable health problem, the worldwide prevalence of subjects with AP is 52%, and 5% at the tooth level incrementing with patients' age (Jiménez-Pinzón et al., 2004; León-López et al., 2022; Tibúrcio-Machado et al., 2021).

The elective treatment for teeth with AP is root canal treatment (RCT). Additionally, the world-wide prevalence of RCT is 8.2%, and the global prevalence of people with at least one RFT is 56% (León-López et al., 2022). RCT outcome has been linked to systemic disease states (Segura-Egea et al., 2023) such as diabetes (Cabanillas-Balsera et al., 2019; Nagendrababu et al., 2020; Segura-Egea et al., 2016) and smoking (Cabanillas-Balsera, Segura-Egea, Bermudo-Fuenmayor, et al., 2020; Cabanillas-Balsera, Segura-Egea, Jiménez-Sánchez, et al., 2020).

It is clearly stablished that under certain circumstances the infection can spread to nearby tissue compartments and may cause a severe fatal inflammatory condition. Taking that into consideration, it can be concluded that AP is not entirely a local episode (Carrotte, 2004). Furthermore, in light of the developing consciousness of a possible link between inflammatory disorders of the oral cavity and disease conditions in other locations, it has also been claimed that acute and chronic manifestations of AP may also be involved (Márton, 2004).

The results of some studies suggest the relationship between periapical inflammation and cardiovascular diseases (Jakovljevic et al., 2020; Jiménez-Sánchez et al., 2020). Moreover, several epidemiological studies have investigated the possible relationship between HTN and AP, with contradictory conclusions (Messing et al., 2019; Segura-Egea et al., 2010). Therefore, it would be interesting to conduct a systematic review to determine whether there is a relationship between AP or RCT and HTN. Knowing whether HTN associates with a greater prevalence of AP or greater RCT failure will allow the dentist to better control hypertensive patients and better monitor their RCT.

The main objective of this systematic review and meta-analysis is to provide a comprehensive overview of the prevalence of AP among hypertensive patients, assessing the potential association between these two conditions. As a secondary objective, the possible relationship of hypertension with the loss of RFT is analysed.

METHODS

Registry protocol

This systematic review is reported in accordance with PRISMA and PRISMA-DTA guidelines (Page et al., 2021) and is registered on PROSPERO (CRD42022302385).

Review question

A specific review question was structured according to the PICO method (population, intervention, comparison and outcome): In adult subjects (P), does the presence of HTN (I) compared to the absence of HTN (C), affect the prevalence of AP, diagnosed radiographically or the survival of RFT (O)? The null hypothesis tested was that there was no significant difference in the prevalence of AP and in the survival of RFT between hypertensive patients and healthy people without hypertension.

Eligibility criteria

The inclusion criteria established were (a) epidemiological studies published until February 2023; (b) studies comparing hypertensive subjects with healthy control, non-hypertensive subjects; (c) studies assessing the prevalence of AP and /or providing data on the prevalence of non-retained RFT, both in hypertensive subjects and in control non-hypertensive subjects. *In vitro* studies, animal studies, case series, studies reporting data only from hypertensive subjects, and studies that had no initial agreement among the reviewers were excluded.

Search strategy and information sources

The selection of the articles was done by three authors individually (J.J.S-E, V.A-Q and C.C-S.). The investigators performed independent electronic searches of PubMed/MEDLINE, Web of Science, Scopus and EMBASE. The search was conducted without filters, language or publication year restrictions and was updated until February 2023. Further manual searches were conducted of the references of the included articles. Articles identified in the searches were screened for eligibility by the three authors by inspection of the title and abstract, or full text if further clarification was necessary. Disagreements on eligibility were resolved by discussion and consensus. Full texts were obtained for all studies meeting the eligibility and inclusion criteria. No filters and limits were considered. In addition, hand searches were performed by considering some periodicals, a references list of some articles, and the grey literature using the databases ProQuest and OpenGrey. After articles were selected, the disagreements among the authors were resolved by consensus (Figure 1).

The terms used for this search were as follows: (Apical periodontitis[Mesh] OR Root filled teeth[Mesh] OR root canal treatment[Mesh] OR Periapical lesion[Mesh] OR Periapical inflammation [Mesh] OR Periapical radiolucency[Mesh] OR Endodontic[All fields]) AND (Cardiovascular disease[Mesh] OR Atherosclerosis[Mesh] OR Hypertension[Mesh] OR Valvular heart disease[Mesh] OR Angina pectoris [Mesh] OR Heart failure [Mesh] OR Acute myocardial infarction[Mesh]).

Risk of bias assessment

To assess the risk of bias in the selected articles, the Cochrane Scientific Committee recommendation was followed (Higgins et al., 2023). Thus, the ROBINS-I tool (Risk Of Bias In Non-randomized Studies – of Interventions)

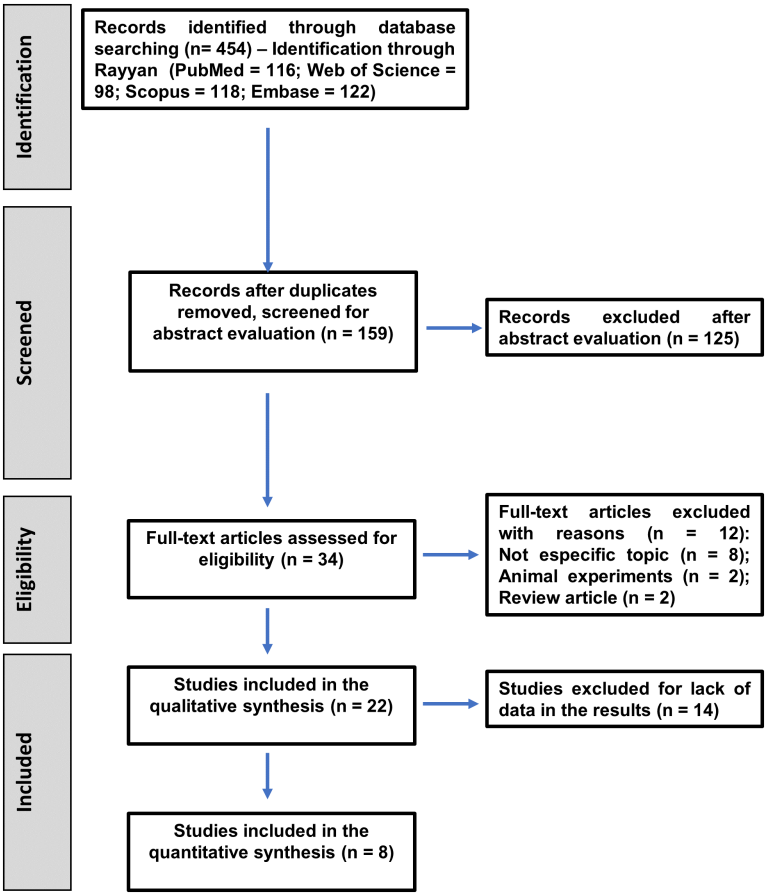

FIGURE 1 Flowchart of the studies included in the systematic review and meta-analysis.

(Sterne et al., 2016) was used. In this tool, the aspects of risk of bias are evaluated individually without assigning scores and are divided into seven domains: random sequence generation, allocation concealment, blinding of outcome assessors, blinding of participants and personnel, incomplete outcome data and selective outcome reporting, comprising the assessment of selection, performance, attrition, reporting and detection bias. Each domain is classified as having a low risk, unclear risk or high risk of bias (Wells et al., 2011). Articles were assessed independently by four reviewers (J.J.S-E., D.C-B., V.A-Q. and C.C-S), and cases of disagreements in the risk of bias were discussed until a consensus was achieved.

Data extraction and analysis

One of the authors (V.A-Q) was responsible for data extraction, while three reviewers (C.C-S, D.C-B and J.J.S-E) verified the tabulated data to ensure the absence of typo errors and carried out the analysis of the articles; the articles in disagreement were discussed. To analyse and synthesize the data, the following details were extracted from the studies: author and year of publication, study design, sample size, objective and results. Pooled estimates from the studies were analysed using a random-effects model meta-analysis. The variables analysed were the prevalence of AP and non-retention of RFT among patients with HTN and non-hypertension control subjects. Forest plots were produced to graphically represent the odds ratio of AP and retention of RFT in both patients with and without HTN. The level of significance was applied to $p = .05$. To determine the heterogeneity among trials, the Tau^2 and the Higgins I^2 test were employed, considering that substantial heterogeneity is considered if I^2 test is higher than 50% (Higgins & Thompson, 2002). The 5.4 RevMan software tool was employed in the statistical analysis (Review Manager (RevMan) [Computer program]. Version 5.4).

Grading of recommendations assessment, development and evaluation

The Grades of Recommendation, Assessment, Development and Evaluation (GRADE) approach (Guyatt et al., 2011) was used for the assessment of the overall quality of the evidence. This procedure defines an initial level of certainty according to the design of the included studies and, subsequently, analyses different domains such as the risk of bias, inconsistency, indirectness, imprecision, publication bias, dose–response gradient, confounding factors or the magnitude of the effect to conclude at a final level of certainty.

RESULTS

The baseline search recovered 454 titles and abstracts found through Rayyan database searching, including 116 from PubMed/ MEDLINE, 98 from Web of Science, 118 from Scopus and 122 from EMBASE. After the removal of duplicates, 159 articles remained, of which 125 were excluded after reading abstract and 34 were selected for full text. After reading the articles in full, 12 were excluded for the following reasons: four did not address AP or RFT as a specific topic (Almoznino et al., 2020; Janket et al., 2014; Nivethitha et al., 2020; Ojehanon & Akhionbare, 2007), three did not have the hypertension as a specific topic (Costa et al., 2014, Donders et al., 2020, Paju et al., 2021), one did not deal any of the specific topics (Bajaj et al., 2012), two were animal studies (Cosme-Silva et al., 2019; Martins et al., 2016) and two were review studies (Sasaki et al., 2016, Verhulst et al., 2019). Twenty-two studies were selected for the qualitative synthesis, but 14 were excluded for not providing the necessary data for meta-analysis (Ahirwar et al., 2021; Almoznino et al., 2021; Assiri et al., 2020; Caplan et al., 2009; Frisk et al., 2003; Gomes et al., 2016; Liljestrand et al., 2016; Meurman et al., 2017; Poornima et al., 2021; Rashmi et al., 2017; Ravikumar et al., 2020; Ruiz et al., 2017; Segura-Egea et al., 2011; Vidal et al., 2016) (Figure 1; Table 1).

Characteristics of the included studies

Finally, eight studies were selected and included for systematic review and meta-analysis (Table 2). Six studies analysed the association between HTN and AP (An et al., 2016; Katz & Rotstein, 2021; Khalighinejad et al., 2017; Messing et al., 2019; Segura-Egea et al., 2010; Yip et al., 2021), and two studies analysed the association between HTN and non-retention of RFT (Mindiola et al., 2006; Wang et al., 2011). Study design, study sample, diagnosis, main results and evidence level of these studies are summarized in Table 2.

Meta-analysis of the prevalence of apical periodontitis

An evidence table was elaborated with data from the included articles (Table 3). The estimated variance between studies was examined using the Tau^2 test and was found to be significant ($\tau^2 = 0.53$; $\chi^2 = 1468.17$; $df = 5$; $p < .01$).

The evidence for heterogeneity ($I^2 = 100\%$) was very high; therefore, the weights of each study were calculated using the random effects model, considering that there

TABLE 1 Studies excluded in the systematic review: excluded reason, authors and year.

Excluded reason	Author (year)
AP, RFT or HTN are not specific topics	Ojehanon & Akhionbare, (2007)
	Bajaj et al. (2012)
	Costa et al. (2014)
	Janket et al. (2014)
	Almoznino et al. (2020)
	Donders et al. (2020)
	Nivethitha et al. (2020)
	Paju et al. (2021)
Animal study	Martins et al. (2016)
	Cosme-Silva et al. (2019)
Review study	Sasaki et al. (2016)
	Verhulst et al. (2019)
Missing data	Frisk et al. (2003)
	Segura-Egea et al. (2011)
	Gomes et al. (2016)
	Liljestrand et al. (2016)
	Vidal et al. (2016)
	Meurman et al. (2017)
	Rashmi et al. (2017)
	Ruiz et al. (2017)
	Caplan et al. (2009)
	Assiri et al. (2020)
	Ravikumar et al. (2020)
	Ahirwar et al. (2021)
	Almoznino et al. (2021)
	Poornima et al. (2021)

was variation between the included studies and allowing the study results to vary in a normal distribution.

The overall OR was calculated using the inverse variance method with random effects, resulting in an OR = 1.73 (95% CI = 0.94–3.21; $p = .08$). The ORs of each study and the pooled OR of the meta-analysis are shown in a forest plot (Figure 2). This result indicates that there is a difference, but not statistically significant, between the prevalence of patients presenting at least one tooth with apical periodontitis and hypertensive or control subjects.

Meta-analysis of the prevalence of non-retention of root-filled teeth

The data from both articles were collected in a table (Table 4). The estimated variance among the two studies was examined by Tau^2 test, resulting non-significant ($\tau^2 = 0.00$; $\chi^2 = 0.76$; $df = 1$; $p = .38$).

Although $I^2 = 0\%$, demonstrating that the studies were very homogeneous, the weights for each study were calculated using the random effects model, allowing study results to vary in a normal distribution. Moreover, statistical homogeneity does not exclude clinical heterogeneity.

The overall OR was calculated using the inverse variance method with random effects, resulting in an OR = 1.78 (95% CI = 1.60–1.98; $p < .00001$). The ORs of both studies and the pooled OR of the meta-analysis are shown in a forest plot (Figure 3). This result indicates that there is a significant difference in the prevalence of extracted RFT between patients with HTN and healthy control subjects.

Publication bias

Publication bias could not be assessed quantitatively as there were fewer than the required minimum of 10 studies (Higgins et al., 2023).

Risk of bias

According to the ROBINS-I tool, of the six studies included for the prevalence of AP, five were classified as low risk of bias, with none or only one domain at high risk of bias, while the other was classified as moderate risk of bias, with two domains at high risk of bias (Messing et al., 2019) (Figure 4). On the other hand, for the prevalence of non-retention of RFT, one study was classified as moderate risk of bias, with two domains at high risk of bias (Mindiola et al., 2006), while the other was classified as low risk of bias, with one of the domains at high risk of bias (Wang et al., 2011) (Figure 5).

GRADE evaluation

Assessment of the overall quality of evidence for each variable analysed was carried out using the GRADE tool, showing in both cases a very low quality of evidence (Figure 6).

DISCUSSION

The aim of this study was to analyse the association between HTN and two endodontic variables, the prevalence of AP and the prevalence of non-retained RFT. For this, a systematic review and meta-analysis were performed,

TABLE 2 Studies on the prevalence of apical periodontitis (AP) and non-retention of root filled teeth (RFT) in hypertensive patients included in the meta-analysis.

Author (year)	Study design	Subjects	Variable	Diagnosis	Main results	Evidence level
Mindiola et al. (2006)	Cross-sectional	Control – 3753 Hypertensive – 424	Retention of RFT	An electronic survey of the dental database from 1991 to 2000	Association $p < .05$ OR: 2.10 CI (1.42–3.11)	4
Segura-Egea et al. (2010)	Cross-sectional	Control – 51 Hypertensive – 40	AP	Periapical	No association $p = .15$ OR: 1.94 CI (0.78–4.81)	4
Wang et al. (2011)	Cross-sectional	Control – 40 024 Hypertensive – 9310	Retention of RFT	An electronic survey of the dental database from 1995 to 2003	Association $p < .05$ OR: 1.75 CI (1.57–1.96)	4
An et al. (2016)	Cross-sectional	Control – 252 Hypertensive – 112	AP	Periapical	No association $p = .26$ OR: 1.29 CI (0.83–2.02)	4
Khalighinejad et al. (2017)	Cross-sectional	Control – 50 Preeclampsia – 50	AP	Panoramic	Association $p = .002$ OR: 2.49 CI (1.1–5.62)	4
Messing et al. (2019)	Cross-sectional	Control – 33 967 Hypertensive – 13 349	AP Endodontic pathology/RFT	An electronic survey of the dental database from 1996 to 2016	Association $p < .0004$ OR: 0.87 CI (0.83–0.91)	4
Katz and Rotstein (2021)	Cross-sectional	Control – 1 414 898 Hypertensive – 265 078	AP Periapical abscess	An electronic survey of the dental database from 2011 to 2020	Association $p < .0001$ OR: 3.12 CI (2.98–3.26)	4
Yip et al. (2021)	Cross-sectional	Control – 11 289 Hypertensive – 4209	AP	An electronic survey of the dental database from 2015 to 2018	Association $p < .0001$ OR: 1.76 CI (1.64–1.89)	4

Note: Study design, subjects and sample size, diagnosis, main results and evidence level.

TABLE 3 Studies about hypertensive patients and the prevalence of AP.

Authors	Year	N° patients	Non-hypertensive control subjects		Hypertensive patients		Odds ratio (95% CI)	*p*
			AP/Total	AP (%)	AP/Total	AP (%)		
Segura-Egea et al.	2010	91	31/51	60.8	30/40	75.0	1.94 (0.78–4.81)	$p = .15$
An et al.	2016	364	121/252	48.0	61/112	54.5	1.29 (0.83–2.02)	$p = .26$
Khalighinejad et al.	2017	100	16/50	32.0	27/50	54.0	2.49 (1.11–5.63)	$p = .03$
Messing et al.	2019	47316	7965/33967	23.4	2805/13349	21.0	0.87 (0.83–0.91)	$p < 0.001$
Katz and Rotstein	2021	1679976	5519/1414898	0.4	3196/265078	1.2	3.12 (2.98–3.26)	$p = .00$
Yip et al.	2021	15498	5216/11289	46.2	2533/4209	60.2	1.76 (1.64–1.89)	$p = .00$
Overall		1743345	18868/1460507	1.29	8652/282838	3.06	1.73 (0.42–3.21)	$p = .08$

Note: Results were extracted and compiled, and descriptive statistics and odds ratios were calculated.

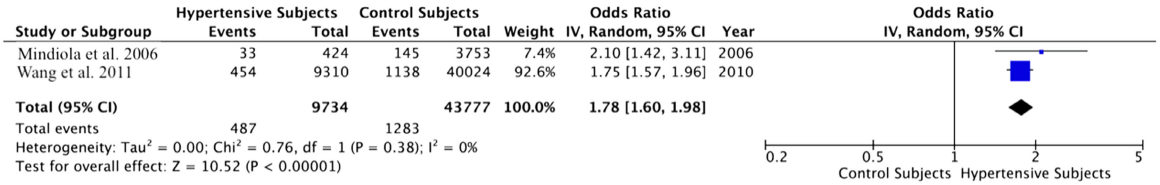

FIGURE 2 Forest plot for the prevalence of apical periodontitis.

TABLE 4 Studies about hypertensive patients and the prevalence of non-retained RFT.

Authors	Year	N° RFT	Non-hypertensive control subjects		Hypertensive patients		Odds ratio (95% CI)	*p*
			RFT*Ext/ Total RFT	RFT*Ext (%)	RFT*Ext/ Total RFT	RFT*Ext (%)		
Mindiola et al.	2006	91	145/3753	3.9	33/424	7.8	2.10 (1.42–3.11)	$p = .0001$
Wang et al.	2011	476	1138/40024	2.8	454/9310	4.9	1.75 (1.57–1.96)	$p < .0001$
Overall		1743457	1283/43777	2.93	487/9734	5.0	1.78 (1.60–1.98)	$p = .00001$

Note: Results were extracted and compiled, and descriptive statistics and odds ratios were calculated.

Abbreviations: RFT, root-filled teeth; RFT*Ext, extracted RFT.

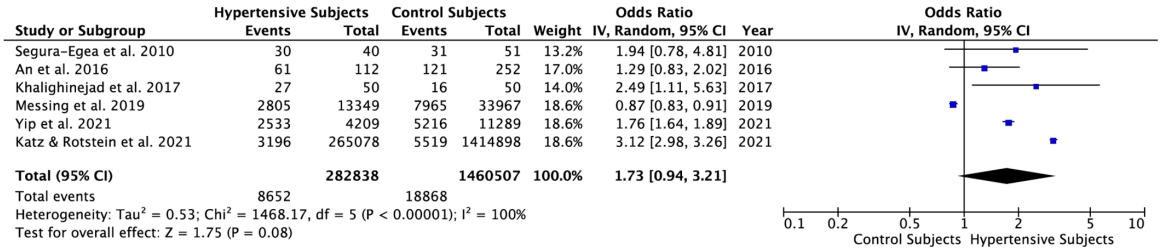

FIGURE 3 Forest plot for the prevalence of non-retention of root-filled teeth.

including the available evidence. The results show that there is no association between the prevalence of AP and HTN. In addition, hypertensive patients have significantly increased odds of losing RFT. However, the quality of the overall evidence has shown a level of certainty very low.

After searching the literature, eight studies were included in the final analysis, six analysing the prevalence of AP (An et al., 2016; Katz & Rotstein, 2021; Khalighinejad et al., 2017; Messing et al., 2019; Segura-Egea et al., 2010; Yip et al., 2021) and two evaluating the prevalence of

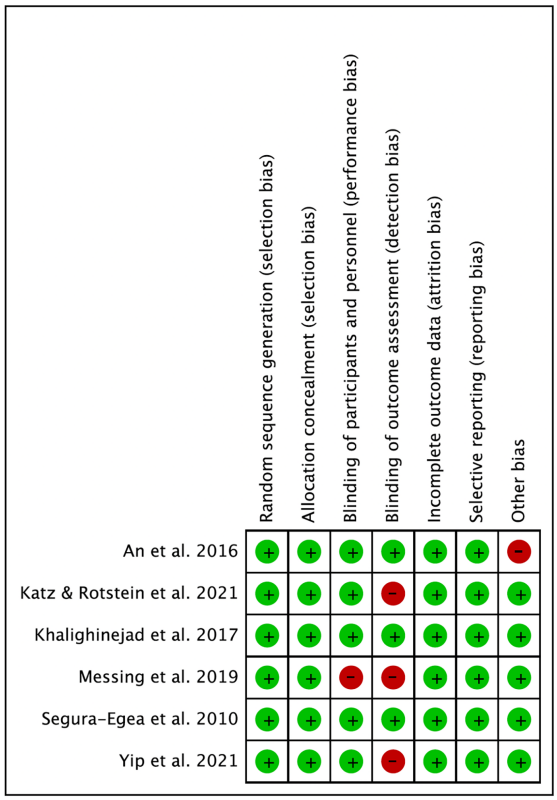

FIGURE 4 Summary of risk of bias assessments for the prevalence of apical periodontitis.

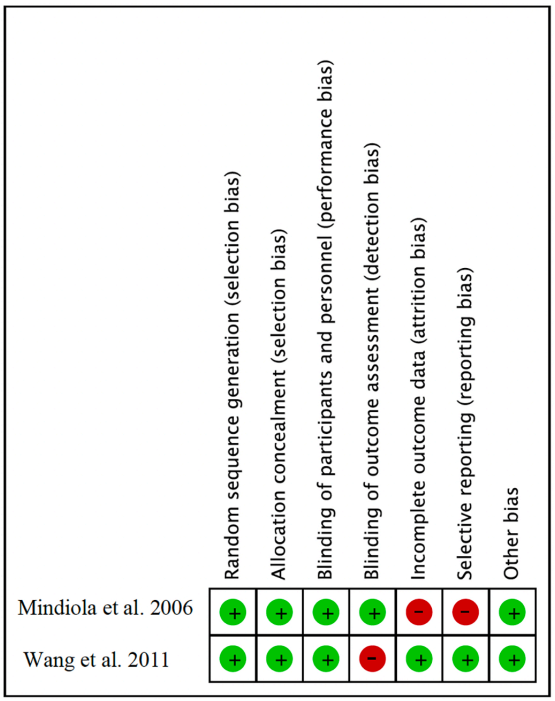

FIGURE 5 Summary of risk of bias assessments for the prevalence of non-retention of root-filled teeth.

non-retention of RFT teeth (Mindiola et al., 2006; Wang et al., 2011). The design of all studies was cross-sectional. Assessment of the risk of bias of the studies for the prevalence of AP shows that although five of the six included studies present a low risk of bias, at least three studies present serious imprecision. This, together with a very serious inconsistency due to the high heterogeneity, degrades the quality of the global evidence using GRADE methodology to a very low certainly.

Very low level of certainty was also obtained for the prevalence of non-retention of root-filled teeth. Despite the included studies showing consistency for this association, the inclusion of only two studies that met the inclusion criteria along with an individual bias presenting one and two high-risk domains downgraded overall certainty.

The first study designed to explore a possible association between endodontic disease variables and coronary heart disease did not find a significant association between periapical disease and HTN (Frisk et al., 2003). The study by Segura-Egea et al. (2010), also found no significant differences in the prevalence of AP in hypertensive patients compared with healthy patients, but the authors say that some factors were not recorded, such as the prevalence of diabetes and smoking habits, which may have confounded the results. The analysis of the extracted data from the study of An et al. (2016) concluded that the prevalence of AP in hypertensive patients was similar to that in control subjects. However, the study showed a statistically significant association between CVD and the number of RFTs.

The third study included in the meta-analysis was conducted by Khalighinejad et al. (2017) provided evidence that pregnant women with undiagnosed/untreated AP are almost two times more likely to develop preeclampsia than pregnant women with no AP. The pre-eclampsia is characterized by HTN and proteinuria after the 20th week of gestation (Backes et al., 2011). One of the most common adverse outcomes of pregnancy and is among the leading causes of maternal mortality (Mammaro et al., 2009). Despite the association found between AP and preeclampsia, the authors emphasize that the data were collected before pregnancy and consider it important to re-evaluate the endodontic status at the end of pregnancy (Khalighinejad et al., 2017), since oral hygiene can be poor during this period (Onigbinde et al., 2014).

Several studies have observed the independent association between AP and inflammatory markers linked to cardiovascular diseases (Gomes et al., 2013; Warner et al., 2004). Systemic elevation of proinflammatory cytokines such as interleukin (IL) 1 beta and tumour necrosis factor alpha has been shown to be a result of AP (Gomes et al., 2013) and initiate structural and functional changes in endothelial cells leading to systemic signs associated with preeclampsia (Roberts et al., 1989).

HTN results from the interaction between genetic and environmental factors (Kato et al., 2015) Is a known

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	[Intervención]	[Comparación]	Relative (95% CI)	Absolute (95% CI)		
Prevalence of apical periodontitis												
6	observational studies	not serious[a]	very serious[b]	not serious	serious[c]	none	8652/282838 (3.1%)	18868/1460507 (1.3%)	**OR 1.73** (0.94 to 3.21)	**9 more per 1000** (from 1 fewer to 27 more)	⨁◯◯◯ Very low	NOT IMPORTANT
Prevalence of non-retention of root filled teeth												
2	observational studies	serious[d]	not serious	not serious	not serious	none	487/9734 (5.0%)	1283/43777 (2.9%)	**OR 1.78** (1.60 to 1.98)	**22 more per 1000** (from 17 more to 27 more)	⨁◯◯◯ Very low	NO IMPORTANTE

CI: confidence interval; **OR:** odds ratio

Explanations

a. Detailed in Fig. 6
b. I2 = 100% and $\tau^2 = 0.53$
c. Segura-Egea et al. 2010, An et al. 2016 and Khalighinejad et al. 2017 include relatively few patients and few events, having a wide confidence interval (CI) around the effect estimate.
d. Detailed in Fig. 7

FIGURE 6 Grade assessment.

major risk factor for CVD, as well as cerebrovascular and renal disease (Warren et al., 2017) and the biggest single contributor to disease and mortality worldwide (Kato et al., 2015). Studies have identified polymorphisms in a variety of disease-relevant genes as significantly associated with HTN (Warren et al., 2017). The study conducted by Messing et al. (2019) carried out a genetic association analysis of AP with known hypertension-associated polymorphisms gene and a trend toward association was found between AP and a polymorphism in the KCNK3 gene. Mutations in this gene can cause idiopathic pulmonary arterial hypertension, a rare disorder characterized by high blood pressure in the pulmonary arteries that can lead to elevated pulmonary arterial pressure, right ventricular failure, and death (Bohnen et al., 2017). Furthermore, studies of chronic periodontitis genes in humans and mouse models have suggested the involvement of other genes whose roles in other systemic diseases are more established (de Vries et al., 2017). This find can explain the results of Messing et al. (2019) which highlight as limitations of the study the cross-sectional design and the use of self-reported information in the dental electronic records, the scarce availability of dental history information on the medical records, and an independent cohort of limited sample size for the genetic association study.

Tiburcio-Machado et al. (2021) compiled data from different communities and reported that 52% of individuals had endodontic disease, without, however, identifying which factors may modify the prevalence of AP worldwide. A subgroup analysis revealed the factors that can influence the prevalence of AP: socioeconomic status of the country; location of recruitment; the systemic conditions; the risk of bias of the primary studies; the image method used and the method used to assess the AP.

Previous studies have found an association between systemic diseases, such as diabetes (Segura-Egea et al., 2019) and cardiovascular diseases (Messing et al., 2019), and some biological mechanisms have been proposed to explain this relationship (Segura-Egea et al., 2015). Also in the case of HTN, some biological mechanisms can be proposed by which it can influence the periapical status. Martins et al. (2016) found that a hypertensive condition leads to higher osteoclastic differentiation, which could influence the endodontic treatment outcome in such a systemic condition. Vidal et al. (2016) reported that the presence of chronic apical periodontitis was associated with higher plasma levels of C reactive protein, interleukin 6, and fibrinogen in a population of severely hypertensive patients. In good accordance with these findings, the results of the cross-sectional study by Katz and Rotstein (2021) indicate that the prevalence of periapical abscesses is significantly higher in hypertensive patients.

Increased calcium secretion has also been observed in hypertensive patients (Tsuda et al., 2001). Another study concluded that primary HTN can significantly reduce the body's bone mineral density (Ye et al. 2017). According to the authors, periapical abscesses are associated with inflammatory processes elicited mainly by microorganisms, it is plausible that existing pathoses can be aggravated by a systemic condition such as hypertension that may also contribute to a delay in bony healing (Katz & Rotstein, 2021). Although, they suggest that the results should be viewed with caution, since they only evaluated the presence of periapical lesions, not considering whether the lesions present were in the healing process. The quality of endodontic treatment and coronal restorations were also not evaluated, and these may be a confounding factor in the results (Katz & Rotstein, 2021).

In the cross-sectional study by Yip et al. (2021), the authors found a higher prevalence of AP associated with TDM2 as well as with an HbA1c higher than 8.0. The data extracted from this study showed a significant association between HTN and AP.

Of the included studies to assess the prevalence of AP in hypertensive patients, only two showed no association (An et al., 2016; Segura-Egea et al., 2010). However, the meta-analysis found no significant differences for the prevalence of AP between hypertensive and healthy patients.

Endodontic treatment is the first choice of treatment for AP. According to Holland et al. (2017) the following factors can affect the healing process of endodontic treatment: biochemical preparation, irrigating solution, intracanal dressing, root canal filling, apical limit of obturation, expansion of the apical foramen and systemic condition. Tooth extraction, non-surgical retreatment and apical surgery are the major events that occur after NSRCT, but tooth extraction is the most common (Chen et al., 2007).

The association of systemic diseases such as DM, HTN, and CVD with tooth extraction after NSRCT has been little explored. The study of Mindiola et al. (2006), an epidemiological study investigating the people who received endodontic treatment from 1991 to 2000 to identify factors affecting the retention of RFT, concluded that DM and HTN isolated contributes to the increase of non-retention RFT. The other included study (Wang et al., 2011) also showed an increased prevalence of non-retention of RFT in hypertensive patients. In fact, the loss of RFT was more prevalent after 2 years in hypertensive patients (Wang et al., 2011).

Limitations and strengths

The results of the present investigation should be evaluated with caution since the study has some limitations.

Although a strength of the study could be the large sample size that was included in the meta-analysis, most of the studies were made from an extensive database, where it is possible that the information was added inaccurately (Katz & Rotstein, 2021; Messing et al., 2019; Mindiola et al., 2006; Wang et al., 2011; Yip et al., 2021).

Quantitative assessment of publication bias proved unfeasible due to an insufficient number of studies in each meta-analysis, falling short of the requisite minimum of 10 (Higgins et al., 2023). This limitation hindered the effective evaluation of funnel plot asymmetry or the execution of more advanced regression-based analyses. Despite the inability to conduct a quantitative analysis of publication bias, it was deemed inconsequential to the overall quality of evidence. Additionally, it is noteworthy that none of the studies incorporated into this review received financial support from the private sector, and none of the authors disclosed any conflict of interest.

Another limitation is that periapical radiography was used in some studies to assess the presence of AP, however, early bone resorptions may not be observed, which may confound the results.

Regarding the risk of bias assessment, it was carried out at the study level, using the ROBINS-I tool (Sterne et al., 2016), in both systematic reviews. Although it was low or moderate, an assessment of the quality of the overall evidence has shown that the level of certainty is quite low. Therefore, it is likely that the real effect is substantially different from the estimated effect, and the contribution of future research studies may lead to clarifying and quantifying more accurately the possible association between HTN and both the prevalence of AP and the prevalence of non-retention of RFT.

Regarding the heterogeneity, for the prevalence of AP, the I^2 value was 100%, indicating high statistical heterogeneity. For this reason, the random effects model has been used to carry out the meta-analysis. However, a distinction must be made between statistical and clinical heterogeneity. In the case of the prevalence of non-retention of RFT, the value of I^2 was zero, meaning that there was no statistical heterogeneity. However, given that the studies were carried out in different centres, logically there was clinical heterogeneity.

Finally, as these are cross-sectional studies, causal conclusions cannot be drawn. The results of this systematic review can only be interpreted in terms of association, not causality. The establishment of mechanistic links between HTN and periapical pathology can only be understood speculatively (Segura-Egea et al., 2019).

Clinical implications

The results of this systematic review have obvious clinical implications, which is why they should be transferred to the daily practice of dentistry. Given the high prevalence of hypertension, it is very common to perform root canal treatments on hypertensive patients. Dentists should be aware of the fact that hypertensive patients face an elevated risk of losing endodontically treated teeth. It is imperative to communicate this heightened risk to patients and to conduct periodic monitoring, paying particular attention to this subset of patients.

CONCLUSIONS

The results of this study suggest that there is no association between the prevalence of AP and HTN. In addition, hypertensive patients have significantly increased odds of losing RFT. However, the quality of the overall evidence has shown a level of certainty very low. More studies, especially

high-quality longitudinal studies, are needed to determine the existence of an association between hypertension and periapical disease or the outcome of root canal treatment.

AUTHOR CONTRIBUTIONS

Conceptualization: Juan J. Segura-Egea, Jenifer Martín-González and Daniel Cabanillas-Balsera; Data curation: Victoria Areal-Quecuty, Cristiane Cantiga-Silva and Juan J. Segura-Egea; Formal analysis: Juan J. Segura-Egea and Daniel Cabanillas-Balsera; Investigation: Victoria Areal-Quecuty and Cristiane Cantiga-Silva; Methodology: Daniel Cabanillas-Balsera, Victoria Areal-Quecuty and Cristiane Cantiga-Silva; Software: Daniel Cabanillas-Balsera; Supervision: Juan J. Segura-Egea; Validation: Juan J. Segura-Egea and Daniel Cabanillas-Balsera; Writing – original draft, Victoria Areal-Quecuty, Cristiane Cantiga-Silva and Daniel Cabanillas-Balsera; Writing – review and editing, Cristiane Cantiga-Silva, Carolina de Barros Morais Cardoso, Luciano Tavares Angelo Cintra and Juan J. Segura-Egea.

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CONFLICT OF INTEREST STATEMENT

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available in PubMed at https://pubmed.ncbi.nlm.nih.gov/. These data were derived from the following resources available in the public domain: SCOPUS, https://www.scopus.com/home.uri.

ETHICS STATEMENT

Not aplicable.

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