

Association between Pulp Stones and Kidney Stones: A Systematic Review and Meta-analysis

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ABSTRACT

Introduction: A systematic review and meta-analysis were performed to evaluate the association between pulp stones and kidney stones. **Methods:** A search for observational studies was performed in PubMed, Scopus, Web of Science, Biblioteca Virtual em Saude, and the gray literature. The Newcastle-Ottawa Scale for Risk of Bias criteria were used to evaluate the internal quality of the included studies. A fixed-effects meta-analysis was performed to evaluate the association between the conditions. **Results:** A total of 213 studies were identified after the removal of duplicates. Of these, 9 studies were selected after screening the titles and abstracts. Finally, after full-text reading for qualitative analysis, 7 studies were selected, and of these, 2 were used in the meta-analysis. A significant association was found between pulp stones and kidney stones (1.97 [95% confidence interval, 1.21-3.18]; $P < .05$). **Conclusions:** This study revealed an association between pulp stones and kidney stones. Further well-designed studies should be conducted in order to confirm whether pulp stones are predictive indicators of undiagnosed kidney stones. (*J Endod* 2019;m:1-7.)

KEY WORDS

Dental pulp calcification; kidney calculi; kidney stones; meta-analysis; pulp stones; systematic review

Pulp stones are regressive alterations in the pulp tissue, and they occur with higher frequency in the pulp chamber. The prevalence of pulp stones can reach up to 50% of surveyed samples¹. The most affected teeth are molars^{1,2}, and females are more affected than males³⁻⁵. Although the prevalence is higher in elderly patients, pulp stones can also be observed in young patients⁵. Commonly, pulp stones are considered incidental findings during imaging examinations² because they are not related to painful symptoms. They occur in healthy teeth and even in unerupted teeth⁶.

Pulp stones can be classified according to their location as follows: "free," which are completely surrounded by pulp tissue; "embedded," which are surrounded by dentin; and "adherent," which are continuous with the dentin. Pulp stones may complicate endodontic treatments, and their removal is often required to improve access to the root canals⁷.

The etiology of this condition has not yet been elucidated⁸. Pulp stones can be derived from the natural process of aging or in response to injuries, such as traumatic occlusion⁹, orthodontic movement¹⁰, and irritant factors that promote chronic inflammation¹¹. Genetic causes¹² and the identification of nanoparticles and nanobacteria have also been mentioned as etiologic factors^{13,14}. Interestingly, these factors have also been associated with kidney stones.

Although some authors have proposed a relationship between pulp stones and kidney stones¹⁵⁻²¹, there is no consistent evidence to show that these conditions are associated. Therefore, this systematic review and meta-analysis aim to answer the following focus question: "Is there an association between pulp stones and kidney stones?"

Pulp stones are alterations commonly found in endodontic practice and have also been suggested as a clinical marker of systemic diseases; however, the existing literature does not fully support the association between pulp stones and kidney stones.

FIGURE 1 - A flow diagram of the study methods.

MATERIALS AND METHODS

The methods described here follow the Meta-analysis of Observational Studies in Epidemiology checklist for meta-analysis of observational studies²².

Protocol Registration

This study was undertaken from August to November 2018 at the Universidade Positivo, Curitiba, Parana, Brazil. Its registration number in the International Prospective Register of Systematic Reviews database is CRD42018109036.

Eligibility Criteria

The focused question was formulated according to the “PECO (population, exposition, comparison, and outcome)” method in which P was the subjects with

permanent teeth, E was pulp stones, C was the presence or absence of pulp stones in permanent teeth, and O was the presence of kidney stones.

Inclusion Criteria

Cross-sectional, case-control, and cohort studies that compared the association between pulp stones in permanent teeth and kidney stones were included.

Exclusion Criteria

The exclusion criteria were as follows:

1. editorial letters, pilot studies, reviews, *in vitro* studies, and descriptive studies, such as case reports and case series, and
2. studies that examined an association between pulp stones and other types of calculi.

Information Sources and Search Strategy

The PECO method guided the search strategy and formulation of the focused question. Within each concept, the controlled vocabulary (Medical Subject Headings terms) and free key words were combined with the Boolean operators “OR” and “AND” ([Appendix 1](#)).

The electronic databases that were searched are also described in [Appendix 1](#). The PubMed search strategy was adapted for each of the databases (Scopus, Web of Science, and Biblioteca Virtual em Saúde). The search was performed considering the population and exposures. To improve the search strategy, the population-related terms included dentition permanent, dental calculus, dental pulp calcification, pulp stones, and dental pulp stone. For exposures, the included terms were kidney calculi, urolithiasis,

TABLE 1 - A Summary of the Studies Selected for This Systematic Review

Study ID	Study design	Country	% of male	Subjects' age mean \pm SD, y (range)	Total number of patients	Types of teeth included	Diagnostic method of kidney stones	Diagnostic method of pulp stones	Dental radiographic evaluation
Aleksova et al ¹⁵	Cross-sectional	Republic of Macedonia	NR	NR \pm NR (20-60)	200	Maxillary and mandibular teeth	Ultrasonography	Panoramic and retromolar radiographies for suspicious teeth	NR
Tarim Ertas et al ¹⁶	Cross-sectional	Turkey	54.31	Kidney stones: 42 \pm NR (20-74) Control: 40 \pm NR (20-69)	232	First and second molars and premolars	History of renal colic confirmed with hematuria and voiding of the calculus, radiographic evidence, or previous surgical and endoscopic removal of stones	Bitewing radiographies	2 experienced dentists
Galav et al ¹⁷	Cross-sectional	India	55.00	NR \pm NR (20-60)	100	NR	Ultrasonography	Panoramic radiography	NR
Kumar et al ¹⁸	Cross-sectional	India	Kidney stones: 56.67 Non-kidney: 52.5	Kidney stones: 33.9 \pm 10.6 (NR) Nonkidney: 34.8 \pm 11.2 (NR)	240	Posterior and anterior teeth	NR	Periapical radiography	2 oral radiologists
Movahhedian et al ¹⁹	Case-control	Iran	45.45	Kidney stones: 44.3 \pm 11.52 (NR) Nonkidney: 41.3 \pm 12.05 (NR)	154	Molars, premolars, and anterior teeth	Ultrasonography	Panoramic radiography	2 oral radiologists
Moudi et al ²⁰	Cross-sectional	Iran	70.00	NR \pm NR (15-50)	130	Posterior teeth	Ultrasonography	Digital bitewing radiography	2 oral radiologists and one endodontist
Patil ²¹	Cross-sectional	Saudi Arabia	Kidney stones: 56.67 Nonkidney: 52.5	Kidney stones: 33.9 \pm 10.6 (NR) Nonkidney: 34.8 \pm 11.2 (NR)	240	Posterior and anterior teeth	NR	Periapical radiography	2 oral radiologists

ID, identification; NR, not reported; SD, standard deviation.

TABLE 2 - A Summary of the Results Reported in the Included Studies in This Systematic Review

Study ID	Number of events/total				Total
	Group with kidney stones and pulp stones/total	Group with kidney stones and nonpulp stones/total	Group without kidney stones and with pulp stones	Group without kidney stones and without pulp stones	
Aleksova et al ¹⁵	70	60	NR	NR	130
Tarim Ertas et al ¹⁶	84	32	86	30	232
Galav et al ¹⁷	20	80	NR	NR	100
Kumar et al ¹⁸	57	63	55	65	240
Movahhedian et al ¹⁹	38	39	28	49	154
Moudi et al ²⁰	36	34	20	40	130
Patil ²¹	57	63	55	65	240

ID, identification; NR, not reported; SD, standard deviation.

nephrolithiasis, kidney stone, renal stone, renal colic, renal calcifications, renal calculi, nephrolith, and urinary lithiasis (Appendix 1).

The reference lists of all primary studies were hand searched for additional relevant publications as were links to related articles of each primary study in the PubMed database. No restrictions were placed on publication date or languages.

The gray literature was inspected in Google Scholar, the System for Information on Grey Literature in Europe, ProQuest Dissertations and Theses Full Text, and the Periodicos Capes databases. In addition, abstracts from the International Association for Dental Research from 1990 to 2018 were searched. The references were managed by EndNote Basic software (Thomson Reuters, New York, NY), and duplicates were removed.

Study Selection and Data Collection Process

The selection process occurred in 2 phases to minimize bias. In phase 1, possible eligible articles were selected by 2 reviewers (R.M.L. and J.S.R.) based on the title and abstract. Any study that did not meet the inclusion criteria was discarded. In phase 2, full-text articles were obtained and classified according to the inclusion criteria by the same reviewers (R.M.L. and J.S.R.). In cases of disagreements regarding inclusion/exclusion criteria, a third

reviewer (L.M.W.) was consulted to finalize the decision.

Pilot-tested, customized extraction forms were used to register the details about the studies, such as study design, participants, diagnostic methods, and results. Each study received an identification number (study ID), which was created by combining the first author's name and the publication year. Information was cross-checked and confirmed for accuracy.

Risk of Bias in Individual Studies

The risk of bias among the included studies was evaluated by 2 independent reviewers (J.S.R. and L.M.W.) using the Newcastle-Ottawa Scale for Risk of Bias (www.ohri.ca/programs/clinical_epidemiology/oxford.asp)^{23,24}.

Discrepancies among the 3 examiners were solved through a consensus. The evaluation criteria yielded a maximum score of 9 points. These score points were divided among the following domains: patient selection (case definition, representativeness of the cases, selection of controls, and definition of controls) for a maximum of 4 points, comparability of groups (comparability of the cases and controls) for a maximum of 2 points, and exposure (ascertainment of exposure, method of ascertainment for cases and controls, and nonresponse rate) for a maximum of 3 points. The studies were later

categorized as a "high risk of bias" (0-3 points), "moderate risk of bias" (4-6 points), and "low risk of bias" (>7 points)²³.

Summary Measures and Synthesis of the Results

Data from eligible studies were classified dichotomously as being present or absent. Only studies classified as low risk of bias were included in the meta-analysis.

A fixed-effects model was selected, and a meta-analysis was performed to estimate the pooled odds ratio for the association between pulp stones in permanent teeth and kidney stones. All analyses were conducted using RevMan 5.3 (Review Manager v. 5.3; The Cochrane Collaboration, Copenhagen, Denmark).

RESULTS

Study Selection

After the database screening and the removal of duplicates, 213 studies were identified (Fig. 1). After screening the titles, 14 studies were left. This was further reduced to 9 studies after the abstracts were examined, and then the full texts were assessed to check eligibility. Among them, 2 were excluded because they were brief reports²⁵ and did not examine the association between pulp stones and kidney stones²⁶ (Appendix 2).

Study or Subgroup	Pulp stones		Non pulp stones		Weight	Odds Ratio M-H, Fixed, 95% CI
	Events	Total	Events	Total		
Moudi et al. (20)	36	54	34	74	40.3%	2.35 [1.14, 4.87]
Movahhedian et al. (19)	38	66	39	88	59.7%	1.71 [0.90, 3.25]
Total (95% CI)		120		162	100.0%	1.97 [1.21, 3.18]
Total events	74		73			
Heterogeneity: Chi ² = 0.42, df = 1 (P = 0.52); I ² = 0%						
Test for overall effect: Z = 2.75 (P = 0.006)						

FIGURE 2 - Forest plots of the association between pulp stones and kidney stones.

Characteristics of Included Articles

All studies included in this review were in English. The characteristics of the 7 selected studies are listed in [Tables 1](#) and [2](#). Six of the studies included in this systematic review were cross-sectional^{15-18,20,21}, and 1¹⁹ was a case-control study.

The countries of origin of the studies are as follows: 2 from India^{17,18}, 2 from Iran^{19,20}, 1 from the Republic of Macedonia¹⁵, 1 from Turkey¹⁶, and 1 from Saudi Arabia²¹.

The percentage of male subjects in the studies ranged from 45%-70%, and only 1 study¹⁵ did not report this information. The age of the participants varied between 15 and 74 years, with the mean being 37.4 years. The number of participants ranged from 100-240.

The type of teeth included in the primary studies varied. Three studies^{18,19,21} included anterior and posterior teeth, 1¹⁵ included maxillary and mandibular teeth, 2^{16,20} included posterior teeth, and 1¹⁷ did not report these data.

The diagnostic method for kidney stones also varied among the studies and included ultrasonography^{15,17,19,20} and a history of renal colic with confirmed hematuria and voiding of the calculus, radiographic evidence of stones, or previous surgical and endoscopic removal of stones¹⁶. Two studies did not report such data^{18,21}.

The diagnostic method for pulp stones used different radiographic techniques and included panoramic and retromolar radiographs for teeth considered to have pulp stones¹⁵, bitewing radiographs^{16,20}, panoramic radiographs^{17,19}, and periapical radiographs^{18,21}.

The professionals who performed the radiographic diagnoses varied widely among the studies, including 1¹⁶ that was performed by 2 experienced dentists, 3^{18,19,21} that were performed by 2 oral radiologists, 1²⁰ that was performed by 2 oral radiologists and an endodontist, and 2^{15,17} that did not report this information.

The results reported in the included studies in this systematic review were as follows: a group with kidney stones and pulp stones, a group with kidney stones and nonpulp stones, a group without kidney stones and with pulp stones, and a group without kidney stones and without pulp stones ([Table 2](#)).

Assessment of the Risk of Bias

The assessment of the risk of bias of the included studies is presented in [Table 3](#). Three studies^{17,18,21} presented a high risk of bias because they did not evaluate the criteria for comparability, and their data analyses were

weak in the areas of patient selection and exposure measurements. Two studies^{15,27} presented a moderate risk of bias because they did not evaluate the criteria for comparability, and they did not meet certain criteria for the data in the areas of patient selection and exposure measurements. Only 2 studies^{19,20} presented a low risk of bias according to the quality assessment Newcastle-Ottawa Scale.

Meta-analysis

A meta-analysis was performed on the studies classified as a low risk of bias^{19,20}. This analysis was based on 2 studies^{19,20} and presented an odds ratio = 1.97 (95% confidence interval, 1.21-3.18; $P < .05$). The results of this analysis showed an association between pulp stones and kidney stones ([Fig. 2](#)). Heterogeneity of the data was not observed (χ^2 test, $P = .52$; $I^2 = 0$).

DISCUSSION

Oral and systemic interrelationships are not a new subject in the dental research field. Some researchers have been focusing on evaluating the associations between several different conditions and oral outcomes^{28,29}. In this context, endodontic medicine, which addresses the associations between endodontic conditions and systemic diseases, has gained prominence. Although it is still controversial³⁰, it has been reported that pulp stones can serve as an important diagnostic marker for systemic diseases⁵.

In the past decade, some studies^{15,16,18-21} have raised the question of whether there is a relationship between pulp stones and kidney stones and examined the association between these 2 conditions. Although a few studies have shown that pulp stones and kidney stones are associated^{15,20} others have failed to demonstrate the same results^{16,18,19,21}. Therefore, the present study aimed to perform a systematic review and meta-analysis with primary studies in order to investigate this association.

Notably, meta-analysis is a quantitative epidemiologic study design. The statistical approach to this method combines the results from multiple studies, instead of undertaking an individual study, in an effort to increase statistical power. This method also serves to resolve reports of uncertainty and disagreement between primary studies and draw a conclusion based on the assessed studies³¹. In the current meta-analysis, an association between pulp stones and kidney stones was observed in which patients with pulp stones were almost twice as likely to present with kidney stones.

An important aspect to be highlighted here is that although 7 studies were initially screened, only 2 were included in the meta-analysis^{19,20} because of the fact that the other studies were considered to have low methodological quality. These facts emphasize the point that future studies should be performed with a focus on the study design in order to decrease the risk of bias.

Another observation in the present systematic review was that all studies were performed in Asian populations¹⁵⁻²¹. This is an important issue that should be carefully discussed because of the possible genetic background that regulates both pathologic calcifications. It is well established that race and genes are implicit in the likelihood of disease risk³², and these results could differ in other populations and ethnic groups. Therefore, more studies that aim to evaluate the association between pulp stones and

kidney stones in different populations are also necessary.

Pathologic calcification is an important subject to be explored in different health research areas. The present study supports the fact that pathologic calcifications share similar etiologic aspects. However, the impact or causality of this relationship cannot be shown here because of the fact that the temporal factor and dose association are not present in the original included studies. Therefore, the connection between them should be further shown through experimental animal studies and observational epidemiologic studies. A recent review in the endodontic medicine field examined the bidirectional relationship between endodontic infections and systemic diseases (33). However, it is possible that the endodontic medicine field is broader, including all endodontic conditions and not only infections.

CONCLUSIONS

Briefly, this study showed an association between pulp stones and kidney stones. Further well-designed studies including cohort studies should be conducted in order to confirm whether pulp stones can predict undiagnosed kidney stones.

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