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PULP STONES AS A POTENTIAL ORAL BIOMARKER OF CARDIOVASCULAR DISEASES: A NARRATIVE REVIEW OF CURRENT GENETIC, RADIOGRAPHIC, AND MOLECULAR EVIDENCE

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ABSTRACT

Background: Pulp stones are calcified masses within the dental pulp, frequently identified as incidental findings on routine dental radiographs. Emerging evidence suggests that these calcifications may reflect broader systemic calcific and inflammatory processes, including those implicated in cardiovascular disease. Because many cardiovascular conditions remain clinically silent in their early stages, radiographic detection of pulp stones may offer a simple, non-invasive avenue for opportunistic cardiovascular risk assessment.

Objective: This review aims to synthesize the genetic, molecular, and radiographic evidence supporting pulp stones as a candidate oral biomarker of cardiovascular disease, with particular attention to their diagnostic relevance in dental imaging.

Methods: Current evidence on pulp stone formation, the molecular pathways shared with cardiovascular calcification, and the clinical-radiographic associations between pulp stones and cardiovascular disease was reviewed, with particular emphasis on studies employing panoramic radiography and cone-beam computed tomography for the detection of pulp calcifications.

Results: Pulp stone formation is driven by chronic inflammation, oxidative stress, dysregulated calcium-phosphate metabolism, and osteogenic signaling pathways—including RUNX2, BMP, Wnt, and inflammatory cytokine-mediated mechanisms—that substantially overlap with those implicated in vascular and valvular calcification. Radiographic studies have consistently reported a higher prevalence of pulp stones among individuals with coronary artery disease, hypertension, hyperlipidemia, and other cardiovascular conditions. Panoramic radiography remains the most practical screening modality given its routine use, low cost, and wide availability, whereas cone-beam computed tomography offers greater sensitivity and three-dimensional localization.

Conclusion: Pulp stones should not be regarded as diagnostic markers of cardiovascular disease; however, their radiographic detection may serve as an adjunctive indicator of systemic calcification risk. Standardized radiographic criteria and prospective studies are needed to establish their clinical utility.

KEYWORDS: Pulp stones, Cardiovascular disease, pulp calcification, Oral biomarkers, Osteogenic signaling.

INTRODUCTION

Cardiovascular disease (CVD) remains one of the foremost contributors to global morbidity and mortality, encompassing coronary artery disease, myocardial infarction, cerebrovascular events, and hypertension [1]. The prevalence of cardiovascular disease is shaped by a complex interplay of modifiable lifestyle factors, including unhealthy dietary patterns, physical inactivity or sedentary behavior, and tobacco exposure, along with genetic predisposition. Metabolic factors such as hypercholesterolemia, hyperlipidemia, and obesity further contribute to cardiovascular risk. In addition, published evidence has recognized periodontal disease as a potential risk factor for cardiovascular diseases [1,2].

The global burden of CVD has risen sharply in recent decades. According to the most recent Global Burden of Disease (GBD) estimates, the number of prevalent CVD cases worldwide more than doubled from approximately 311 million in 1990 to 626 million in 2023, while annual cardiovascular deaths increased from 13.1 million to 19.2 million over the same period [1]. Projections suggest this burden will continue to grow substantially, with global cardiovascular prevalence estimated to rise by as much as 90% between 2025 and 2050, driven largely by population growth and ageing [3].

The burden of CVD is disproportionately high in low- and middle-income countries, where limited access to healthcare and preventive services compounds the problem. Because many cardiovascular conditions remain clinically silent in their early stages, diagnosis is often delayed, increasing the risk of adverse events. Collectively, CVDs account for a substantial share of global deaths and disability-adjusted life years (DALYs), placing considerable strain on health systems worldwide [2]. Public health strategies that promote awareness, healthier lifestyles, and improved access to care remain central to addressing this burden.

Early identification of at-risk individuals is therefore essential for limiting disease progression and improving clinical outcomes. Established cardiovascular biomarkers-cardiac troponins, B-type natriuretic peptide (BNP), inflammatory markers, and advanced imaging have substantially improved diagnostic and prognostic accuracy, but their cost, invasiveness, and limited availability in resource-constrained settings restrict widespread use [4]. This has prompted interest in more accessible indicators of cardiovascular risk, including oral findings such as pulp stones [5] and nutrient canals [6], and has reinforced the value of interdisciplinary approaches to a disease as multifactorial as CVD.

Given the growing recognition of oral-systemic health interactions, pulp stones have emerged as candidate indicators of systemic calcific and inflammatory processes. Clarifying their biological features and underlying molecular mechanisms may help establish whether they can serve as a practical oral biomarker of cardiovascular disease. This review therefore examines the current genetic and molecular evidence linking pulp stone formation to cardiovascular pathology.

METHODOLOGY

This article was conducted as a narrative review synthesizing the current genetic, molecular, and clinical-radiographic literature examining pulp stones and their proposed association with cardiovascular disease. A comprehensive literature search was performed using three major electronic databases-PubMed, Scopus, and Google Scholar-covering publications from January 2000 to February 2026.

Search terms were derived from Medical Subject Headings (MeSH) and free-text keywords, including "pulp stones," "dental pulp calcification," "pulp calcification," "cardiovascular disease," "coronary artery disease," "vascular calcification," "atherosclerosis," "hypertension," "osteogenic differentiation," "biomarker," "panoramic radiography," and "cone-beam computed tomography." These terms were combined using the Boolean operators AND and OR to construct comprehensive search strings ("pulp stones" OR "dental pulp calcification") AND ("cardiovascular disease" OR "coronary artery disease" OR "vascular calcification") in order to capture the broadest body of relevant literature.

The search was restricted to articles published in the English language. Titles and abstracts were screened for relevance to the genetic, molecular, or radiographic association between pulp stones and cardiovascular disease, and the full texts of potentially eligible articles were retrieved and reviewed in detail. Reference lists of key articles, including previous reviews and meta-analyses, were also manually screened to identify additional relevant studies not captured by the database searches.

Because this review followed a narrative rather than a systematic methodology, no protocol was registered in advance, and a formal risk of bias assessment was not undertaken. The included studies varied considerably in design—ranging from in vitro and histopathological investigations to cross-sectional and case-control studies, systematic reviews, and meta-analyses—and were synthesized qualitatively to provide a comprehensive, narrative overview of the genetic, molecular, and clinical evidence linking pulp stones to cardiovascular disease.

Biology and Pathogenesis of Pulp Stones

Pulp stones, also termed dental pulp calcifications, are classified according to their mode of formation and location within the pulp chamber. The principal subtypes include:

1. **True pulp stones:** composed of dentin-like tissue and typically associated with odontoblastic activity, the process responsible for dentin formation.
2. **False pulp stones (dystrophic calcifications):** mineral deposits that arise independently of odontoblast activity, generally reflecting degenerative changes within the pulp.
3. **Free pulp stones:** unattached masses lying freely within the pulp chamber, variable in size and shape.
4. **Attached pulp stones:** calcified masses adherent to the pulp chamber wall or adjacent dentin, often associated with chronic irritation or inflammation.
5. **Embedded pulp stones:** calcifications entirely enclosed within pulp tissue and detectable only on histological sectioning [7].

Characterizing these subtypes is relevant not only to their dental implications but also to their possible association with systemic conditions such as cardiovascular disease, with which they may share underlying pathophysiological mechanisms.

Mechanisms of Pulp Calcification

Pulp calcification is a multifactorial process involving the progressive deposition of mineralized material within pulp tissue. Although the precise mechanisms remain incompletely defined, current evidence implicates aging, chronic inflammation, tissue injury, genetic predisposition, and dysregulated mineralization pathways in the onset and progression of pulp stone formation [8]. These factors drive the differentiation of pulp cells toward osteoblast-like or odontoblast-like phenotypes, resulting in ectopic mineral deposition within the pulp chamber [9].

According to the prevailing model, calcification is initiated around a nidus such as degenerating cells, collagen fibers, thrombi, or necrotic debris that provides a scaffold for the deposition of calcium and phosphate crystals. Local tissue injury from dental caries, restorative treatment, trauma, or orthodontic forces may accelerate this process by inducing sustained inflammatory responses within the pulp [10].

Inflammation is central to pulp stone formation. Pro-inflammatory cytokines—interleukin (IL)-1β, IL-6, and tumor necrosis factor-alpha (TNF-α)—activate mineralization-related signaling and upregulate osteogenic markers such as runt-related transcription factor 2 (RUNX2), alkaline phosphatase (ALP), and osteocalcin, thereby enhancing the osteogenic differentiation potential of dental pulp stem cells and promoting calcified deposit formation [11].

Oxidative stress similarly contributes to pulp calcification: excess reactive oxygen species (ROS) can activate nuclear factor-kappa B (NF-κB) signaling, sustaining inflammation and promoting aberrant mineralization. Comparable mechanisms operate in vascular calcification, pointing to biological pathways shared between dental pulp and cardiovascular tissue [12].

Additional regulatory input comes from growth factor signaling. Bone morphogenetic proteins (BMPs), transforming growth factor-beta (TGF-β), and Wnt/β-catenin signaling promote odontogenic and osteogenic differentiation of pulp cells, and their upregulation may favor excessive mineral deposition. Genetic variation in genes governing dentin formation and mineral metabolism—including DSPP, DMP1, COL1A1, and RUNX2 may further modulate individual susceptibility to pulp calcification [13].

Calcifying nanoparticles (CNPs), formerly referred to as nanobacteria, have also been implicated in pulp stone formation. These self-propagating, sub-micron mineral-protein complexes can be visualized within pulp stones by immunohistochemical and immunofluorescence staining and have been isolated and cultured from the majority of dental pulp stone specimens examined, suggesting that CNPs may act as a nidus that initiates and propagates ectopic mineral deposition within the pulp [14]. In parallel, osteopontin, a non-collagenous phosphoprotein normally involved in regulating bone and dentin mineralization, has been immunolocalized within the organic matrix of human pulp stones alongside type I collagen, osteonectin, and osteocalcin, indicating that pulp cells actively synthesize and deposit mineralization-regulating proteins during stone formation rather than undergoing purely passive calcification [15]. Because osteopontin is similarly upregulated within calcified atherosclerotic plaques and vascular smooth muscle cells undergoing osteogenic transdifferentiation, its presence in pulp stones offers additional molecular evidence linking dental pulp calcification with the mechanisms of cardiovascular calcification.

Collectively, pulp calcification arises from a convergence of inflammatory, oxidative, degenerative, and mineral-regulatory processes that closely parallel pathological calcification in cardiovascular tissue, lending biological plausibility to the proposed link between pulp stones and cardiovascular disease [16]. Figure 1 describes the mechanisms of pulp calcification.

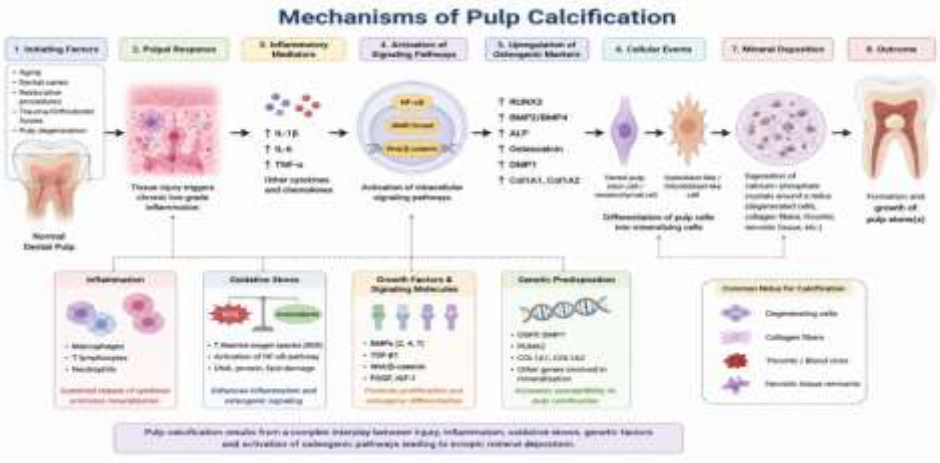

Figure 1. Mechanisms of pulp calcification.

Genetic and Molecular Basis of Pulp Stone Formation

Pulp stone formation is increasingly understood as an actively regulated biological process rather than a passive, age-related degenerative change. It reflects the coordinated activation of osteogenic signaling, inflammatory mediators, and genetic factors that together drive ectopic mineral deposition within the dental pulp. Notably, several of the molecular pathways implicated in this process-spanning inflammation, oxidative stress, and osteogenic differentiation-overlap substantially with those governing vascular calcification, providing a mechanistic basis for evaluating pulp stones as an oral biomarker of cardiovascular risk.

i. Osteogenic Signaling Pathways

Osteogenic signaling governs osteoblast differentiation and bone formation through a coordinated network of signaling molecules and transcription factors. Central to this network are bone morphogenetic proteins (BMPs), Wnt signaling, and RUNX2, the master regulator of osteoblast differentiation and skeletal development. RUNX2 directs the commitment of mesenchymal stem cells to the osteoblastic lineage and controls the transcription of key osteogenic genes, including osteocalcin and alkaline phosphatase [17]. BMP2 and BMP4, members of the TGF-β super family, promote differentiation of mesenchymal stem cells into osteoblasts via Smad-mediated signaling, driving transcription of osteogenic genes [9].

This osteogenic response is further modulated by systemic factors such as inflammation and metabolic disturbance, which can influence both pulp stone formation and its relevance as a cardiovascular biomarker. Elevated inflammatory cytokines, for example, can disrupt normal osteogenesis and promote aberrant calcification in soft tissues, including dental pulp [18]-

an observation of particular relevance in conditions such as chronic kidney disease, where ectopic calcification is markedly exacerbated [19].

ii. Inflammatory Pathways

Chronic inflammation is a principal driver of pulp stone formation. Inflammatory cells responding to caries, trauma, restorative intervention, or age-related pulp degeneration release cytokines that promote mineralization, most notably IL-1β, IL-6, and TNF-α.

IL-1β stimulates expression of mineralization-related genes and promotes differentiation of dental pulp stem cells into odontoblast-like cells; sustained IL-1β signaling may enhance calcified matrix deposition. IL-6 similarly sustains chronic inflammation and upregulates bone-associated proteins, facilitating pulp mineralization [20]. TNF-α contributes to tissue injury and repair by activating osteogenic transcription factors such as RUNX2, thereby influencing the cellular differentiation and matrix remodeling associated with pulp calcification [21].

Collectively, these cytokines establish a pro-calcific microenvironment that favors mineralizing cell phenotypes. Because IL-1β, IL-6, and TNF-α are also key mediators of vascular inflammation and calcification, their shared role suggests a plausible molecular link between pulp stones and cardiovascular disease [22].

iii. Oxidative Stress and Calcification

Oxidative stress, arising when ROS production overwhelms antioxidant defenses, is an important contributor to pathological calcification in the dental pulp. Aging, inflammation, trauma, and pulp degeneration all increase ROS generation within the pulp microenvironment.

Beyond causing direct cellular damage, ROS act as signaling molecules that promote osteogenic differentiation and mineral deposition, upregulating calcification-related genes and driving transformation of pulp stem cells toward mineralizing phenotypes [23]. A key mechanistic link is ROS-induced activation of NF-κB signaling, which sustains cytokine production (IL-1β, IL-6, TNF-α) and perpetuates chronic inflammation, thereby promoting expression of osteogenic markers such as RUNX2 and alkaline phosphatase and facilitating ectopic mineral deposition within the pulp [12]. Because ROS generation and NF-κB activation are also established drivers of vascular inflammation and calcification, these shared pathways provide further biological support for the proposed association between pulp stones and cardiovascular calcification [23].

iv. Candidate Genes Associated with Pulp Calcification

Several genes governing dentin formation, extracellular matrix organization, and mineral metabolism have been implicated in pulp stone development (Table 1). Although the genetic architecture of pulp calcification remains incompletely characterized, current evidence suggests that alterations in genes regulating odontogenesis and mineral metabolism may confer susceptibility to ectopic pulp mineralization.

Dentin sialophosphoprotein (DSPP), a principal non-collagenous protein in dentin mineralization, is highly expressed by odontoblasts and essential to dentin matrix formation; its mutation or dysregulation has been linked to abnormal dentin mineralization and may contribute to pulp calcification [24].

Dentin matrix protein-1 (DMP1) regulates calcium and phosphate homeostasis and odontoblast differentiation, and its increased expression has been linked to enhanced mineral deposition and calcified tissue formation within the pulp [25].

Collagen type I alpha 1 (COL1A1), the principal structural protein of the dentin extracellular matrix, influences matrix organization and mineralization; given its central role in connective tissue integrity, altered COL1A1 expression may create a microenvironment favorable for calcification and contribute to pulp stone development [18].

RUNX2, a master regulator of osteogenic differentiation, stimulates expression of mineralization-related proteins such as alkaline phosphatase and osteocalcin, promoting ectopic calcification. Its implication in both dental pulp and vascular calcification positions RUNX2 as a particularly important molecular link between the two processes [23].

Collectively, these genes regulate matrix formation, odontoblast differentiation, and mineral deposition; their dysregulation may underlie pathological pulp calcification and provide a genetic basis for its association with systemic calcification disorders, including cardiovascular disease.

Table 1. Key genes associated with pulp stone formation and their biological functions in mineralization pathways.

Gene	Primary Function	Potential Role in Pulp Calcification
DSPP	Dentin matrix mineralization	Promotes dentin and pulp mineral deposition
DMP1	Biomineralization and phosphate regulation	Enhances odontogenic differentiation and calcification
COL1A1	Extracellular matrix formation	Provides scaffold for mineral deposition
RUNX2	Osteogenic transcription factor	Drives osteogenic differentiation and ectopic calcification

Shared Molecular Mechanisms Between Pulp Stones and Cardiovascular Disease

Accumulating evidence indicates that pulp stone formation and cardiovascular calcification share overlapping molecular and cellular mechanisms. Both represent actively regulated mineralization processes rather than passive calcium deposition, and are driven by chronic inflammation, oxidative stress, dysregulated mineral metabolism, and osteogenic signaling, providing biological plausibility for their observed association.

i. Pathological Calcification as a Common Process

Pathological calcification involves the abnormal deposition of calcium-phosphate crystals within soft tissue. In the dental pulp, this manifests as discrete or diffuse pulp stones; in the cardiovascular system, it occurs within the vascular wall, cardiac valves, and atherosclerotic plaques. Despite their anatomical differences, both settings involve cellular differentiation toward mineralizing phenotypes, extracellular matrix remodeling, and activation of shared calcification pathways, suggesting that pulp stones may represent a localized expression of a broader systemic tendency toward ectopic calcification [16].

ii. Inflammation and Endothelial Dysfunction

Chronic inflammation underlies both pulp and vascular calcification. Cytokines such as IL-1β, IL-6, and TNF-α drive tissue remodeling and osteogenic gene expression in both settings. Within the vasculature, sustained inflammation contributes to endothelial dysfunction, a key step in atherogenesis and vascular calcification; the identification of similar inflammatory mediators in calcified pulp tissue suggests a shared pro-calcific microenvironment [26].

iii. Oxidative Stress

Oxidative stress links pulp and cardiovascular calcification through common signaling pathways. Excess ROS promotes cellular injury and activates NF-κB signaling, which enhances expression of pro-inflammatory cytokines and osteogenic markers and thereby facilitates ectopic calcification. These pathways are well established in vascular calcification and are increasingly recognized in the pathogenesis of pulp calcification [12].

iv. Dysregulated Calcium–Phosphate Metabolism

Maintaining calcium-phosphate homeostasis is essential for normal tissue mineralization, and its disruption can lead to inappropriate mineral deposition in soft tissues. In cardiovascular disease, this manifests as vascular and valvular calcification; comparable disturbances in local mineral availability, extracellular matrix composition, and calcification-promoting proteins may similarly influence pulp stone formation, suggesting that pulp calcification could reflect broader systemic alterations in mineral metabolism [27].

v. Osteogenic Transformation Pathways

A shared hallmark of pathological calcification is the acquisition of osteoblast-like characteristics by resident cells, marked by upregulation of transcription factors and mineralization-related proteins, including RUNX2, alkaline phosphatase, osteocalcin, and BMPs. Activation of these pathways in both dental pulp and vascular tissue promotes extracellular matrix mineralization and further supports the concept that dental pulp calcification may indicate systemic cardiovascular pathology [28].

Figure 2 demonstrates the shared molecular pathways linking pulp stones and cardiovascular diseases.

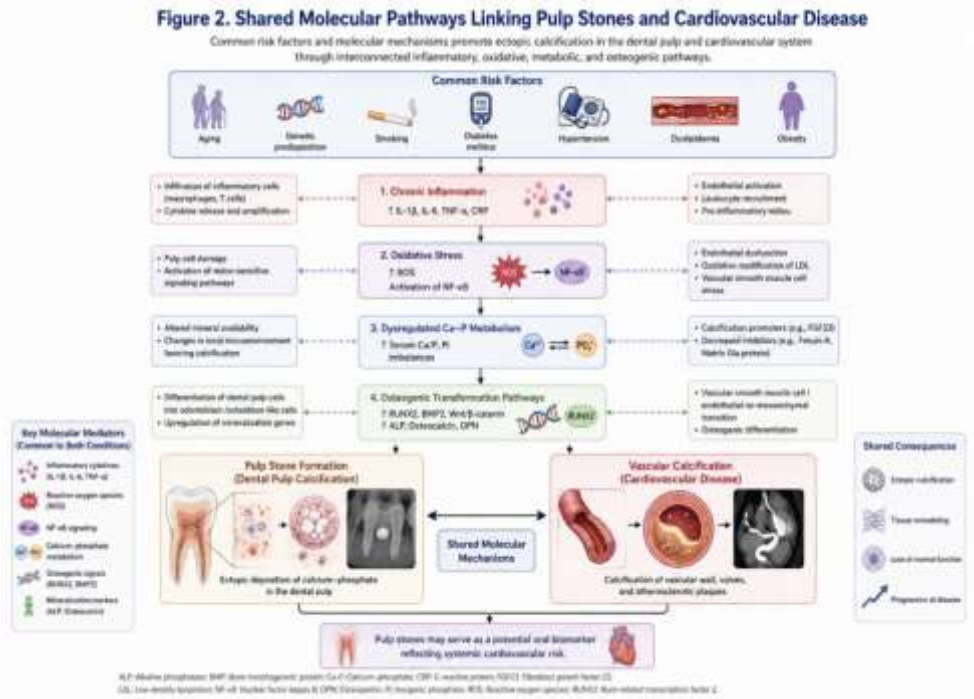

Figure 2. Shared molecular pathways linking pulp stones and cardiovascular disease.

Evidence Linking Pulp Stones and Cardiovascular Disease

A growing body of clinical and epidemiological evidence supports an association between pulp stones and cardiovascular disease (CVD), with several studies reporting a higher prevalence of pulp stones among individuals with cardiovascular conditions relative to healthy controls, consistent with the hypothesis that pulp calcification reflects a systemic predisposition to pathological mineralization [29-33]. Coronary artery disease (CAD) is the most extensively studied cardiovascular condition in this context. Multiple studies using panoramic radiography and advanced imaging have demonstrated a significantly higher prevalence of pulp stones among patients with confirmed CAD, consistent with shared mechanisms—chronic inflammation, oxidative stress, and osteogenic signaling—contributing to both coronary and pulp calcification [34]. Case-control studies using bitewing radiography have reported similar findings in patients with coronary artery disease and ischemic heart disease, with near-universal pulp stone prevalence and a substantially greater number of calcified deposits than in age- and sex-matched healthy controls, further supporting the value of routine dental radiographs in identifying individuals with underlying coronary pathology [35,36]. Hypertension has similarly been associated with increased pulp stone occurrence in several observational studies, potentially reflecting the chronic vascular injury, endothelial dysfunction, and low-grade systemic inflammation characteristic of hypertension, which may promote ectopic calcification in both vascular tissue and the dental pulp. The available evidence, however, remains limited, and further study is required [8]. Atherosclerosis, a progressive inflammatory disease characterized by calcification of the arterial wall and atherosclerotic plaques, has also been examined in this context. The co-occurrence of pulp stones with carotid artery calcification and other markers of systemic atherosclerosis has prompted speculation that pulp calcification may indicate underlying vascular disease. Although a direct causal relationship has not been established, the shared molecular pathways involved provide a strong rationale for further investigation [37]. Radiographic assessment remains the principal method for detecting pulp stones and evaluating their cardiovascular relevance. Panoramic radiography, owing to its widespread availability in routine dental practice, is the most commonly used modality in this literature; several studies report a higher prevalence and greater number of pulp stones among cardiovascular patients, raising the possibility of opportunistic cardiovascular screening during routine dental examination [30]. Cone-beam computed tomography (CBCT) offers superior sensitivity and three-dimensional visualization relative to conventional radiography, and recent CBCT-based studies report a higher prevalence of pulp stones than earlier panoramic-based estimates, suggesting that conventional imaging may underestimate their true occurrence [38]. Direct evidence linking CBCT-detected pulp stones to cardiovascular disease, however, remains limited.

Overall, the available literature offers preliminary but reasonably consistent support for an association between pulp stones and cardiovascular disease across populations and imaging modalities, reinforced by biological plausibility from shared inflammatory, oxidative, and osteogenic mechanisms. Not all findings are concordant, however: a recent large retrospective study found the highest pulp stone prevalence among systemically healthy controls rather than among patients with cardiovascular disease, underscoring the multifactorial nature of pulp calcification and the need for cautious interpretation of the existing evidence [33]. Several additional limitations nonetheless warrant caution: most studies are cross-sectional and cannot establish causality; sample sizes are frequently small; diagnostic criteria for pulp stones vary across studies; and confounders such as age, diabetes, and smoking are not consistently controlled. Longitudinal data assessing whether pulp stones predict future cardiovascular events are also lacking. Well-designed prospective studies are therefore needed before the clinical utility of pulp stones as a cardiovascular biomarker can be established.

Table 2. Clinical and radiographic studies evaluating the association between pulp stones and cardiovascular disease [5,29-38].

Study	Country	Study Design	Sample Size	Cardiovascular Condition	Imaging Method	Key Findings
Ezoddini-Ardakani et al., 2011 [29]	Iran	Case-control	61	Coronary artery stenosis	Panoramic radiography	Pulp stones were present in 82% of patients with coronary stenosis versus 48% of controls (OR 4.83; 95% CI 1.5–15.4).
Khojastepour et al., 2013 [30]	Iran	Cross-sectional	122	Ischemic cardiovascular disease	Panoramic radiography	Higher prevalence of pulp calcifications among patients with ischemic cardiovascular disease, suggesting a potential screening role for dental radiographs.
Babu et al., 2020 [36]	Saudi Arabia	Case-control	300 (150 CAD/150 controls)	Coronary artery disease	Bitewing radiography	CAD patients showed 100% pulp stone prevalence versus 90% in controls, with markedly more calcified deposits (2217 vs 639) in the CAD group ($p<0.05$).

Srivastava et al., 2020 [38]	Saudi Arabia	Cross-sectional (CBCT-based)	229 (73 CVD/76 DM/80 controls)	Cardiovascular disease and type 2 diabetes mellitus	Cone-beam computed tomography	Tooth-wise prevalence was highest in the cardiovascular group (16.65%) versus the diabetic (9.01%) and control (3.86%) groups; CVD conferred a 2.94-fold higher risk of pulp stones than controls (95% CI 1.54–3.10).
Shivanna et al., 2020 [34]	India	Cross-sectional	CAD patients and controls	Coronary artery disease	Panoramic radiography	Patients with CAD exhibited a higher prevalence of pulp stones, supporting their potential as a cardiovascular risk indicator.
Jawahar et al., 2021 [39]	India	Hospital-based prevalence study	70	Hypertension and hyperlipidemia	Radiographic and histopathological evaluation	Irregular and non-laminated pulp stones were significantly associated with hypertension and hyperlipidemia.
Nachiappan et al., 2021 [35]	India	Case-control	300 (150 IHD/150 controls)	Ischemic heart disease	Bitewing radiography	IHD patients exhibited 100% pulp stone prevalence with significantly more calcified deposits than matched healthy controls, supporting early radiographic screening for IHD.
Almadhoon et al., 2022 [31]	Systematic review and meta-analysis	9 eligible studies	—	Cardiovascular disease	Multiple imaging modalities	Meta-analysis demonstrated a significant association between pulp stones and cardiovascular disease, with notable heterogeneity among studies.
Parashar et al., 2022 [32]	Systematic review and meta-analysis	10 studies	—	Cardiovascular disease	Multiple imaging modalities	CVD patients were approximately 4.3 times more likely to exhibit pulp calcifications than controls (OR 4.30; 95% CI 2.19–8.46); certainty of evidence rated low.
Vieira et al., 2023 [37]	Systematic review and meta-analysis	Multiple studies	—	Atherosclerotic (carotid) calcification	Multiple imaging modalities	Meta-analysis found a significant association between pulp stones and calcified atherosclerotic plaques, reinforcing pulp stones as a marker of systemic vascular calcification.
Hasan et al., 2025 [5]	India	Cross-sectional	200	Cardiovascular disease	Digital panoramic radiography	Cardiovascular disease was the strongest predictor of pulp stones (OR 7.38; 95% CI 5.20–10.47).
Gökyar et al., 2025 [33]	Turkey	Cross-sectional (retrospective)	400 (100 each: CVD, DM, CVD+DM, controls)	Cardiovascular disease and type 2 diabetes mellitus	Digital panoramic radiography	Overall pulp stone prevalence was 59.5%, but was highest among healthy controls (69%) rather than CVD (60%) or CVD+DM (65%) groups, indicating no consistent elevation with CVD and underscoring the multifactorial nature of pulp stone formation.

As summarized in Table 2, evidence linking pulp stones to cardiovascular disease has accumulated steadily over the past decade. Early work by Ezoddini-Ardakani et al. demonstrated a significantly higher prevalence of pulp stones among patients with angiographically confirmed coronary artery stenosis than among individuals with normal coronary arteries. Subsequent studies extended these findings to ischemic cardiovascular disease, coronary artery disease, hypertension, and hyperlipidemia, consistent with pulp calcification reflecting systemic calcific processes [39]. More recently, Hasan et al. identified cardiovascular disease as the strongest predictor of pulp stones among several chronic systemic conditions examined, and two independent systematic reviews and meta-analyses published in 2022 concluded that individuals with cardiovascular disease are significantly more likely to exhibit pulp calcifications than healthy controls—although the overall certainty of evidence remains low owing to methodological heterogeneity and a predominance of observational study designs.

Pulp Stones as a Cardiovascular Biomarker

The accumulating evidence linking pulp stones to cardiovascular disease has generated interest in their potential utility as an oral biomarker of cardiovascular risk. Because pulp stones are readily identifiable on routine dental radiographs, they represent a non-invasive, cost-effective finding that may offer insight into underlying systemic calcification processes [4]. Although their clinical significance remains under investigation, the molecular overlap between dental pulp and vascular calcification supports the concept that pulp stones could indicate susceptibility to cardiovascular disease.

This biological plausibility is reinforced by the extent of shared mechanisms between pulp and vascular mineralization, suggesting that pulp stones may reflect a systemic predisposition to pathological calcification rather than representing an isolated dental finding. Because panoramic radiographs are already obtained as part of routine dental care, they offer an opportunity to detect pulp stones without additional cost or radiation exposure. Identification of multiple or extensive pulp calcifications could alert dental practitioners to possible underlying cardiovascular risk and facilitate timely medical referral for further evaluation [30]. While pulp stones cannot presently be regarded as a diagnostic marker of cardiovascular disease, they may contribute to risk stratification when interpreted alongside established cardiovascular risk factors, potentially serving as an adjunctive indicator of systemic calcification that helps identify individuals who may benefit from comprehensive cardiovascular assessment [31-32]. Most available studies investigating this relationship are cross-sectional or case-control in design, leaving the temporal relationship between pulp stone formation and cardiovascular events unclear [31-32]. Large-scale prospective cohort studies are needed to determine whether pulp stones can predict the future development of cardiovascular disease.

Considerable methodological variation—in imaging modality, diagnostic threshold, and classification system—also contributes to heterogeneity across studies and limits comparison between them [40]. The development of standardized diagnostic criteria and reporting guidelines will be essential before pulp stones can be reliably incorporated into cardiovascular risk assessment strategies.

In summary, current evidence supports the potential of pulp stones as a novel oral biomarker of cardiovascular disease, though further longitudinal and mechanistic studies are required to establish their clinical utility and predictive value.

Future Directions

Despite accumulating evidence linking pulp stones to cardiovascular disease, substantial knowledge gaps remain. Future research should prioritize clarifying the molecular basis of pulp calcification, validating its clinical relevance, and exploring its integration into precision healthcare frameworks.

Advances in molecular biology offer new avenues for elucidating the mechanisms connecting pulp stones and cardiovascular calcification. Transcriptomic analyses could identify gene expression signatures associated with pulp mineralization and reveal pathways shared with vascular calcification, while proteomic approaches may help characterize protein biomarkers and molecular mediators common to both processes [4].

Multi-omics approaches—integrating genomics, transcriptomics, proteomics, and metabolomics—may provide a more comprehensive understanding of the biological networks underlying pulp stone formation, potentially identifying novel biomarkers, therapeutic targets, and molecular signatures relevant to cardiovascular risk [4].

Artificial intelligence (AI) and deep learning have shown considerable promise for the automated detection of radiographic abnormalities. Future AI-based systems could enable rapid, accurate identification of pulp stones on panoramic and CBCT imaging, supporting large-scale screening and risk assessment; integrating such image analysis with clinical and demographic data may further enhance the predictive value of pulp stones as indicators of cardiovascular disease [41].

The growing recognition of oral-systemic health interactions supports the incorporation of dental findings into broader healthcare strategies. If validated through future research, pulp stones may serve as a readily accessible imaging biomarker for cardiovascular risk assessment, and their inclusion in personalized risk-prediction models could strengthen interdisciplinary collaboration between dental and medical professionals, contributing to earlier identification of individuals at increased cardiovascular risk.

CONCLUSION

Pulp stones are increasingly recognized as more than incidental radiographic findings and may represent a manifestation of broader systemic calcification processes. Current evidence indicates that pulp calcification shares several molecular and genetic pathways with cardiovascular calcification, including chronic inflammation, oxidative stress, dysregulated mineral metabolism, and osteogenic signaling.

Clinical and epidemiological studies have consistently reported a higher prevalence of pulp stones among individuals with cardiovascular disease, supporting a potential association between the two conditions. Given their frequent, incidental

detection on routine dental radiographs, pulp stones may offer an inexpensive and non-invasive opportunity for opportunistic cardiovascular risk identification within dental settings.

However, current evidence is derived largely from observational studies, and important limitations remain regarding causality, standardization, and predictive value. Well-designed longitudinal studies, combined with advanced molecular and multi-omics investigations, are needed to clarify the biological relationship between pulp stones and cardiovascular disease and to determine whether pulp stones can be established as a reliable oral biomarker of cardiovascular risk.

As precision medicine continues to evolve, dental radiographic findings such as pulp stones may emerge as valuable components of integrated oral-systemic health assessment, helping bridge dentistry and cardiovascular disease prevention.

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