

A Professional Courtesy of:



Raaed Batniji, DMD • Nermine Batniji, DDS
Samir Batniji, DDS

Your ENDODONTIC SPECIALTY

www.endodontic.net

1111 Grand Ave., Ste. D
Diamond Bar, CA 91765
909-396-9944 • Fax: 909-396-9984

1111 W. Covina Blvd., Ste. 130
San Dimas, CA 91773
909-592-9197 • Fax: 909-592-8860

9353 Fairway View Place, Ste. 210
Rancho Cucamonga, CA 91730
909-945-5008 • Fax: 909-581-6668



Endodontic Inflammatory Disease and Myocardial Infarction

Among well-established risk factors for cardiovascular disease, chronic inflammation contributes to the development of atherosclerosis, a major factor in the development of cardiovascular disease, a leading cause of death worldwide. Endodontic inflammatory disease naturally results from the bacterial assault on the pulp in carious teeth. Untreated, this can lead to pulp necrosis, which in turn leads to apical periodontitis. Although root canal treatment may result in the healing of periapical tissue and a concomitant reduction in inflammation, many endodontically treated teeth still show signs of persistent or recurrent periapical inflammation.

Because of the influence of systemic inflammation on cardiovascular disease, several studies have investigated its possible link with dental inflammation. However, study results have been inconsistent and somewhat contradictory, possibly due to the difficulty controlling for other established cardiovascular disease risk factors. To resolve this question, Sebring et al from the University of Gothenburg, Sweden, undertook an analysis of evidence obtained in a multi-

year case-control study designed to investigate links between marginal periodontitis and the incidence of a first myocardial infarction (MI).

Over a 4-year period, patients ≤ 75 years of age and who had recently suffered a first MI were recruited for the study. Each patient was matched by sex, age and geographical area to a control who had not suffered a previous MI or undergone heart valve replacement. Demographics and health histories, including family histories of cardiovascular disease, were collected. The periodontal status of both patients and controls was determined from panoramic radiographs, which were assessed for

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- the number of remaining teeth
- the number of decayed teeth
- the number of root-filled teeth
- the number of teeth with periapical lesions

Periapical lesions were further classified as primary periapical lesions (in nonroot-filled teeth) or secondary periapical lesions (in root-filled teeth). A decayed, missing and filled tooth

(DMFT) score was calculated for each patient and control.

In 797 patients and 796 controls, the number of missing teeth and the percentage of missing teeth were significantly associated with an increased risk of a first MI. A significant association was also seen in the group of patients limited to those aged <60 years for the number of decayed teeth, the presence of any decayed teeth and the proportion of decayed teeth, and the risk of a first MI; however, the presence of any decayed teeth in patients aged ≥60 years did not correlate with an increased risk. In patients aged <65 years, the presence of a primary periapical lesion was significantly associated with a first MI. Patients with filled teeth free of decay had a decreased risk of a first MI.

Conclusion

Given the association of untreated caries, periapical lesions and root fillings with a first MI, endodontic inflammatory disease may be a contributing factor to patient susceptibility for cardiovascular disease. In contrast, patients who have undergone successful dental treatment may reduce their risk for cardiovascular disease.

Sebring D, Buhlin K, Norhammar A, et al. Endodontic inflammatory disease: a risk indicator for first myocardial infarction. *Int Endod J* 2022;55:6-17.

Treatment Options For Necrotic Immature Teeth

Thin, fragile dentin walls, interrupted root formation and apical arrest of the wide-open apex against root filling material make endodontic treatment of necrotic immature teeth difficult. Standard treatment involves apexification with biocompatible materials, frequently mineral trioxide aggregate (MTA).

An MTA plug allows for greater root development but does not increase the thickness of the dentinal walls, leaving them prone to fracture. Regenerative endodontic treatment (RET), an alternative to apexification, aims to restore tissue architecture and biological function of damaged tissue by generating new tissue similar to the original tissue through the survival of stem cells adjacent to the apical forame. Ideally, RET encourages bone healing and allows for root maturation, including apical closure and dentinal wall thickening.

However, evaluation of RET outcomes requires subjective scoring systems that fail to establish accurate, repeatable results. Aricioglu et al from Recep Tayyip Erdoğan University, Turkey, sought to resolve this problem through the use of fractal analysis, which permits the characterization of tissue architecture and detection of potential abnormalities without interpretation by

a human evaluator. Thus, they could evaluate the newly generated trabecular bone architecture and compare levels of periapical healing in cases treated with either an MTA plug or RET.

They analyzed results from patients aged 15 to 40 years without any systemic disease who had been treated over a 4-year period at a university clinic for immature, necrotic permanent teeth that had periapical radiolucent lesions ≤5 mm and a wide apical foramen >1 mm, which required apexification of a single root with a single canal. Periapical radiographs for 15 teeth treated with an MTA plug and the same number of teeth treated with RET were evaluated at the 1-year follow-up to determine the size of the lesion; the same radiographs were used for the fractal analysis.

Both groups showed a significant reduction in lesion size after 1 year; no significant difference was seen between the groups. Similarly, the fractal analysis showed a significant increase in mean values at 1-year follow-up for both groups, and again, no significant difference between the groups were found (Table 1).

Conclusion

Both the MTA plug and RET showed satisfactory resolution of periapical radiolucencies in >85% of cases studied. Both procedures provide satisfactory outcomes when treatment includes properly sealed

Table 1. Comparison of results between MTA plug and RET groups.

	Periapical lesion area (in pixels)			Fractal dimension values		
	MTA plug	RET	p value	MTA plug	RET	p value
Pre-op value	0.80 ± 1.35	1.64 ± 2.26	.163	1.22 ± 0.09	1.22 ± 0.11	.925
1-year follow-up value	0.10 ± 0.12	0.22 ± 0.30	.220	1.33 ± 0.07	1.30 ± 0.10	.309
p value	<.001 ^a	<.001 ^a		<.001 ^a	<.001 ^a	

^aStatistically significant.

apical barriers and the proper use of disinfection procedures. The choice of treatment should be determined by an experienced practitioner on a case-by-case basis.

Aricioglu B, Gunacar DN, Kosar T, et al. Assessment of bone quality of apical periodontitis treated with MTA plug and regenerative endodontic techniques. Aust Endod J 2022;doi:10.1111/aej.12697.

Chronic Systemic Medications and Endodontic Disease

Studies conducted over recent decades have established an association between endodontic disease and systemic disorders, including diabetes mellitus, cardiovascular disease, renal disease, gastrointestinal disease, human immunodeficiency virus infection and rheumatoid arthritis. Treatment of these conditions often includes the chronic administration of powerful drugs, which clinically affect the pathogenesis or healing of pulpitis and apical periodontitis.

The use of biological medications for the management of chronic inflammatory diseases, such as anti-tumor necrosis factor alpha (anti-TNF- α), has positive effects on the progression of apical periodontitis with an enhanced healing response to endodontic treatment, while a similar trend has been seen in patients receiving long-term anti-TNF- α treatment for inflammatory bowel disease.

Alghofaily from King Saud University, Saudi Arabia, and Fouad from the University of Alabama at Birmingham conducted a systematic review of

relevant clinical studies to identify connections between long-term medication use and endodontic outcomes. The 12 studies that met the inclusion criteria involved a range of medications, including

- statins
- monoclonal antibodies to receptor activator of nuclear factor kappa B ligand (RANKL)
- monoclonal antibodies to TNF- α
- metformin
- bisphosphonates
- denosumab
- glucocorticoids

Included in the review were randomized clinical trials, along with human cohort, case-control, cross-sectional, prospective and retrospective studies, that reported the effects of systemic medications on the incidence or prevention of irreversible pulp pathosis or apical periodontitis, pulp calcification, cervical root resorption and endodontic treatment outcomes. All studies included control groups and lasted ≥ 1 year.

One large study of patients taking metformin and statins found independent associations of each medication with a lower odds ratio and a lower prevalence of apical periodontitis. Metformin demonstrated an ability to increase the healing and lower the progression of apical periodontitis. The positive effect of statins on bone formation comes as a result of stimulating the expression of anabolic factors, including vascular endothelial growth factor and bone morphogenetic protein 2. This may, however, also be at the root of an association of statins with pulp calcification. A similar increase in pulp calcification was

found in long-term transplantation patients taking different immunosuppressive or corticosteroid medications.

In a study of patients with osteoporosis, treatment with bisphosphonates demonstrated a beneficial effect against bone loss. In contrast, patients taking glucocorticoids were at greater risk of bone abnormalities and reduced bone density.

Conclusion

The authors of this systematic review concluded that the heterogeneity of study designs and the low level of evidence severely limited their conclusions. Better designed future studies may help practitioners understand correlations between chronic systemic medications and endodontic disease.

Alghofaily M, Fouad AF. Association of chronic systemic medications with the incidence, prevalence, or healing of endodontic disease: a systematic review. J Endod 2022;48:1458-1467.

Re-treating Canals Filled With Tricalcium Silicate-based Sealer

Persistent periapical periodontitis may require nonsurgical re-treatment of the root canal. Because any previous filling materials left on canal walls may harbor microorganisms that can lead to re-treatment failure, success necessitates the entire removal of the existing root canal filling materials. Nonsurgical re-treatment options, such as ultrasonic instruments, nickel-titanium (NiTi) rotary files, passive ultrasonic irrigation (PUI) and solvents, have dem-

onstrated varying levels of success in removing root-canal filling materials.

However, several recent developments in endodontic treatment have created new questions concerning the technique. In particular, a novel tricalcium silicate-based sealer (iRoot SP/EndoSequence BC Sealer) demonstrates favorable biocompatibility and antibacterial properties. Yet, because of their chemical properties, tricalcium silicate-based sealers are most frequently used with a single-cone technique, which means there is a larger amount of sealer in the canal. One study showed that re-treated canals originally filled with tricalcium silicate-based sealers had more residual filling materials; another showed that the sealer and/or the gutta-percha could not be completely removed by instrumentation and ultrasonic irrigation, resulting in canals that retained more debris in the apical third.

One proposed solution involves photon-initiated photoacoustic streaming (PIPS), a technique using a low-energy erbium:yttrium-aluminum-garnet (Er:YAG) laser to activate the irrigant in the root canal, thereby allowing it to penetrate deeper. PIPS has been shown to be more effective than syringe-based irrigation and ultrasonic activation at removing the smear layer and debris in teeth. Based on these results, Yang et al from Sun Yat-sen University, China, investigated the use of PIPS to determine if the technique might prove a better way to remove tricalcium silicate-based sealer.

The researchers used 36 extracted human teeth with completely developed apices and a single straight root canal. After identical preparation of the root canals, the teeth were filled using the single-cone technique with

Table 2. Median volume of residual filling materials (in mm³) removed by the final technique.

	Syringe-based irrigation	Passive ultrasonic irrigation	Photon-initiated photoacoustic streaming
Coronal	0.03	0.02	0.10
Middle	0.01	0.10	0.14
Apical	0.01	0.07	0.06
Overall	0.03	0.14	0.30

tricalcium silicate-based sealer and gutta-percha, and stored for 2 weeks to allow complete sealer setting. Root canals were then re-treated using rotary files with the crown-down technique but without solvent.

The teeth were divided into 3 groups, each of whose root canals were irrigated with 2.5% sodium hypochlorite (NaOCl) and 17% ethylenediaminetetraacetic acid (EDTA):

- **Group 1 (classic syringe-based irrigation):** no further action was taken; this group served as the negative control
- **Group 2 (PUI):** the irrigants were activated using an ultrasonic tip
- **Group 3 (PIPS):** the irrigants were activated using an Er:YAG laser

After treatment, all teeth were scanned using micro-computed tomography and scanning electron microscopy (SEM) to determine the amount of filling materials removed and the cleanliness of the root canal walls.

The remaining filling material was significantly less for Groups 2 and 3 than for Group 1, with PIPS outperforming PUI in the coronal third (Table 2). SEM revealed that in the apical and middle thirds, a thick smear layer and filling debris covered nearly all the canal walls in Group 1. In the PUI group, some dentinal tubes were open, while 50% to 75%

of dentinal tubes in the apical and >75% in the middle third were open in the PIPS group.

Conclusion

While none of the techniques fully eliminated filling debris throughout the entire length of the canal, PIPS performed significantly better in teeth originally restored with tricalcium silicate-based sealers and gutta-percha.

Yang R, Han Y, Liu Z, et al. Comparison of the efficacy of laser-activated and ultrasonic-activated techniques for the removal of tricalcium silicate-based sealers and gutta-percha in root canal retreatment: a microtomography and scanning electron microscopy study. BMC Oral Health 2021;21:275.

In the next issue:

- Association of pulp stones to cardiovascular and renal diseases
- Biomechanical behavior and life span of maxillary molar

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