IEJ
Iranian Endodontic Journal

Apical Periodontitis in Vital and Nonvital Teeth: Clinical and Radiographic Features

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Article Type: **Review Article**

Received: 11 Feb 2024
Revised: 14 May 2024
Accepted: 23 May 2024
Doi: *10.22037/iej.v19i3.45605*

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Apical periodontitis (AP) is a common inflammatory condition predominantly caused by the response of the immune system to microbial invasion within the root canal system. Contrary to conventional perception, AP may occur in vital teeth with inflamed pulp; adding complexity to diagnosis and treatment. AP, due to its frequent lack of symptoms and reliance on radiographic evaluation for detection, often presents diagnostic challenges. In addition, AP pathogenesis involves complex interactions between microbial virulence and host immune response at the cellular and molecular levels. Comprehensive diagnostic procedures, including patient history, clinical examination, and radiographic evaluation, are essential for early detection and necessary intervention, with the recognition of clinical signs and symptoms underscoring the importance of regular dental evaluations. The current review primarily discusses the radiographic and clinical features of AP in vital and non-vital teeth; introducing a new taxonomic classification to improve diagnostic precision and treatment outcomes. Moreover, it proposes different treatment categories/options for the management of AP, based on pulp status as well as clinical and radiographic findings; emphasizing vital pulp therapy and root canal treatment for vital and non-vital teeth with AP, respectively. Furthermore, the global and regional epidemiology of AP is presented, along with its association with systemic health conditions; *e.g.*, cardiovascular diseases, diabetes mellitus, and adverse pregnancy outcomes. Moreover, future research directions are advocated to improve the efficacy and predictability of diagnosis and treatments; paving the path for clinicians in early detection, accurate diagnosis, and effective management of AP to enhance oral health outcomes.

Keywords: Apical periodontitis; Diagnosis; Endodontics; Periapical Lesions, Pulpotomy; Vital Pulp Therapy

Introduction

Apical periodontitis (AP) stands as a prevailing inflammatory condition chiefly attributed to microbial intrusion within the root canal system, a concept pioneered by Kakehashi et al. in 1965 [1] and further delineated by Bergenholtz [2] and Sundqvist [3]. Unlike dental caries and periodontal diseases, which often exhibit overt clinical symptoms, AP frequently adopts a silent behavior, rendering its accurate diagnosis a challenging endeavor. This inherent subtlety of AP, in addition to the necessity for differential diagnosis between it and nonodontogenic radiolucent periapical lesions, complicates its identification, often necessitating reliance on radiographic examinations for its detection [4, 5]. However, this dependency on radiographs may inadvertently obscure or underestimate its true prevalence, particularly in asymptomatic cases, thus highlighting the complexity inherent in diagnosing AP.

It is important to note that AP can occur in both non-vital and vital teeth [6], which complicates its diagnosis and treatment. Consequently, there arises a crucial necessity to comprehensively understand the periapical health status across diverse populations [7]. Such comprehension not only facilitates early detection and intervention but also empowers policy-makers to judiciously allocate resources for the prevention and treatment of endodontic maladies, thereby fostering improved overall oral health-related quality of life [8].

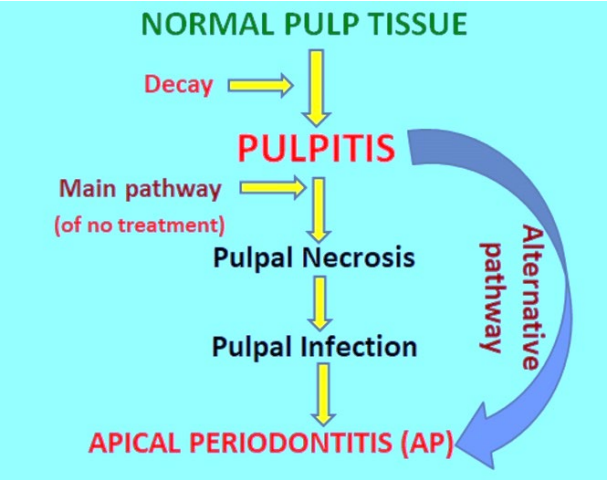

Figure 1. Two pathways from the onset of pulp inflammation (pulpitis) to the development of AP can be delineated: the predominant pathway, where pulpal inflammation progresses to pulp necrosis and subsequent infection, leading to the development of AP because of the immune response, and an additional pathway, where the pulp remains vital but inflamed, yet AP still occurs. This latter scenario may arise from a mild but continuous microbial attack that, while not severe enough to cause pulp necrosis, is sufficient to trigger the inflammatory processes leading to AP.

Moreover, it is essential to emphasize that this review primarily focuses on primary AP in both vital and non-vital teeth that have not undergone endodontic treatment and subsequently failed. Furthermore, we predominantly focus on treatment modalities for vital teeth with pulp exposures, including those experiencing pulpitis and AP. Thus, the overarching aim of this review is to provide comprehensive insights into the clinical/radiographic features of AP in non-vital teeth, with a special emphasis on vital teeth, thereby shedding light on its multifaceted manifestations and complexities.

Nomenclature and Classification

Nomenclature

AP, interchangeably termed periapical periodontitis or periradicular periodontitis, constitutes a spectrum of inflammatory conditions affecting the periapical tissues surrounding the root apex. This expansive terminology encompasses various pathological manifestations, including periapical granuloma, periapical cyst, periapical disease, periapical inflammation, radicular cyst, or radicular granuloma [9].

Classification Systems

The World Health Organization has delineated five primary types of AP, encompassing acute and chronic forms, periapical abscesses with or without sinus involvement, and radicular cysts [10]. However, this classification, while comprehensive, overlooks the structural aspects and histological states of periapical lesions. In response to this limitation, Nair proposed an alternative classification grounded in histopathology and lesion dynamics [11]. This alternative framework integrates stringent criteria for each entity, including the distribution of inflammatory cells, presence of epithelial cells, cyst formation, and the lesion's relationship to the apical foramen.

It is imperative to underscore that the clinical diagnosis of pulp and periapical diseases presents formidable challenges due to the variability in symptoms and histological presentations. Attempts to correlate clinical signs with histological findings have often resulted in ambiguity, emphasizing the imperative for revised and more comprehensive classification systems to enhance diagnostic precision and treatment efficacy [12].

Definition

Clinically, AP presents as inflammation of the periodontium encircling the root apex, usually linked with microbial infection and the production of toxic by-products [13]. This cascade, triggered by either indirect or direct microbial infiltration of the dental pulp tissue, results in pulp inflammation and/or necrosis. Subsequently, it instigates the deterioration of periapical tissues and bone resorption, affecting both vital and non-vital teeth (Figure 1). This intricate pathology underscores the complexity inherent in diagnosing and treating AP.

Bacterial Pathogenesis in Apical Periodontitis

The pathogenesis of AP is a dynamic interplay between microbial invaders and host immune responses [14]. In non-vital teeth, microbial intrusion from the root canal initiates acute AP, characterized by severe pain and tooth tenderness. Polymorphonuclear leukocytes (PMNs) initiate an acute inflammatory response, often resulting in rapid radiographic evidence of bone resorption [15]. Chronic AP arises from prolonged exposure to microbial stimuli, transitioning from a phase dominated by neutrophils to one rich in macrophages, lymphocytes, and plasma cells. Chronic lesions often indicate a "lull phase" following acute inflammation, where T-lymphocytes and macrophages play significant roles in down-regulating inflammation and promoting tissue repair [16].

Bacterial Colonization and Biofilms

Bacteria adhere to dentinal walls, forming biofilms that initiate pulpal inflammation prior to exposure. Upon exposure, severe inflammation ensues as bacteria colonize exposed tissue, leading to necrosis and invasion of the root canal. The composition of the

microbiota evolves as the disease progresses, with virulent strains and bacterial synergy contributing to acute infections [12].

Virulence Factors

Members of the endodontic microbiota produce a plethora of virulence factors contributing to pathogenicity [15]. Enzymes like proteinases, hyaluronidase, and DNases degrade extracellular matrix components, facilitating bacterial spread and tissue damage. Exotoxins such as leukotoxin cause cell membrane damage and cell death, exacerbating tissue destruction. Bacterial components like lipopolysaccharides, peptidoglycan, and bacterial DNA drive tissue damage and inflammation. Additionally, bacterial peptide N-Formyl-Methionyl-Leucyl-Phenylalanine serves as a chemoattractant for immune cells, aiding bacterial invasion. Heat-shock proteins modulate host cell activities in response to environmental stress, influencing inflammation and cell death. Metabolic end-products like volatile sulfur compounds and short-chain fatty acids are toxic to host cells, compromising host defense mechanisms and exacerbating tissue damage.

Research on the pathogenesis of AP in vital teeth is immature/ongoing, necessitating further evidence to confirm analogous patterns in this context.

Pathogenesis at the Cellular and Molecular Level

Cellular Response

PMNs play a pivotal role in inflammation but can also induce tissue damage through enzyme release [17]. Lymphocytes, including T-cells (Th1 and Th2) and B-cells, regulate immune responses, with plasma cells producing antibodies. Macrophages, activated by microorganisms, participate in antigen presentation, cytokine secretion, and inflammation modulation through mediators like interleukin (IL)-1 and tumor necrosis factor (TNF)-α. Osteoclasts resorb bone, while epithelial cells, including epithelial rests of Malassez, proliferate under cytokine influence, contributing to radicular cyst pathogenesis [18].

Molecular Mechanisms

Bacterial complex lipids, Pro-inflammatory and chemotactic cytokines like IL-1, IL-6, IL-8, and TNF promote leukocyte adhesion, lymphocyte activation, and bone resorption [19, 20]. Interferons (IFNs) exhibit antiviral properties, with IFN-γ, IFN-α, and IFN-β contributing to immune modulation [21]. Colony-stimulating factors regulate hematopoietic cell proliferation, while growth factors like transforming growth factor (TGF)-β stimulate macrophages, fibroblasts, and angiogenesis. Eicosanoids, including prostaglandins (PG) and leukotrienes (LT), exert pro-inflammatory effects, activating osteoclasts and attracting neutrophils [22]. Effector molecules like matrix metalloproteinases degrade extracellular matrix components, exacerbating tissue destruction [23]. Antibodies, predominantly immunoglobulins, participate in antimicrobial defense, though antigen-antibody complex formation may augment pathogenicity.

Incidence and Epidemiology

Global Incidence

The global incidence of AP exhibits notable inconsistency influenced by various factors such as age, education level, access to dental care, and diagnostic methodologies used across different regions [7, 24, 25]. Case-controlled studies and epidemiological surveys are primary methodologies for investigating the outcomes of root canal therapy (RCT). While case-controlled studies often report higher success rates within university clinics, epidemiological surveys encompass treatments administered by both specialists and general practitioners, providing more representative success rates. These investigations contribute to a comprehensive understanding of AP distribution and prevalence [24], guiding advancements in diagnostic techniques, treatment modalities, and post-treatment care.

Systematic reviews have highlighted the variability in AP prevalence rates, which range widely from 16-86%, underscoring the complex interplay between socioeconomic determinants, healthcare infrastructure, and oral health outcomes. Interestingly, the results of two different meta-analyses reveal a global AP prevalence of 52% among adults, emphasizing the substantial burden it imposes on individuals and healthcare systems worldwide [7, 25]. Subsequent subgroup analyses of the recent systematic review provide nuanced insights into the socio-economic, medical, and methodological determinants of AP incidence, highlighting the need for targeted interventions to address this significant public health concern. Efforts to raise awareness, promote oral hygiene practices, and foster collaborative partnerships among stakeholders are crucial steps toward reducing the burden of AP and improving overall oral health-related quality of life globally.

Incidence in Specific Regions

In Iran, a cross-sectional survey revealed that 52% of endodontically treated teeth displayed AP [26]. The study emphasized the critical role of root canal treatment quality in determining periapical health, with teeth receiving acceptable RCT showing a lower prevalence of AP compared to those with

unacceptable RCT. This underscores the importance of quality assurance in endodontic treatments and highlights potential areas for improvement in clinical practice. Similarly, other regional studies, like the one mentioned above, offer insights into the high prevalence rates of AP across various geographic regions [27, 28]. These studies focus on identifying factors influencing AP incidence, providing valued data for researchers and healthcare policymakers to develop targeted interventions.

Association with Systemic Health Conditions

AP has been linked with various systemic health conditions, highlighting the broader implications of this localized dental condition. Understanding these associations is critical for comprehensive patient care/informing targeted interventions.

Cardiovascular Diseases

Pulpitis and AP can elicit systemic responses similar to other microbial inflammations through bacteria and bacterial products, such as lipopolysaccharides, leading to increased release of inflammatory mediators. Although the inflammation area in AP is relatively small, systemic phenomena can occur but are generally limited. Asymptomatic lesions of endodontic origin (ALEO), however, might still impact the elevated levels of inflammatory mediators [29, 30].

Research has shown that untreated primary lesions are more commonly associated with cardiovascular diseases than treated ALEOs [31]. Additionally, there are possible links between the presence of endodontic lesions and cardiovascular conditions. A significant issue in many studies is the lack of consideration for past smoking habits, a crucial factor in cardiovascular diseases, even though current smoking status is often recorded [32].

Despite these limitations, it seems reasonable to conclude that AP could significantly increase inflammatory parameters. The exact effect of such an increase remains unknown. Although the association between ALEOs and various systemic disorders is not firmly established, it is conceivable [33, 34]. Future research should focus on this relationship and its consequences, including the impact of RCT on these associations, making it a significant study topic [35]. Moreover, it is crucial to note that the existence of an association does not imply causality. Just because two events coincide does not mean one causes the other.

Diabetes Mellitus

Diabetic patients may present with a higher prevalence of periapical lesions [36, 37], delayed periapical repair, larger osteolytic lesions, and poorer outcomes for root-filled teeth. Poor periapical status correlates with higher HbA1c levels in type 2 diabetic patients, suggesting a potential link between glycemic control and periapical health. The compromised immune function and impaired wound healing characteristic of diabetes may contribute to the increased susceptibility to periapical infections and delayed healing in diabetic individuals.

Smoking and Other Systemic Diseases

The association between smoking and endodontic infection remains controversial [38], with conflicting evidence regarding its impact on the prevalence and outcomes of AP and RCT. However, hypertension, osteoporosis, inherited coagulation disorders, and chronic liver disease are systemic conditions that may influence the prevalence and outcomes of AP and RCT [39]. These systemic diseases can affect immune function, tissue healing, and inflammatory responses, potentially influencing the development and progression of periapical infections.

Adverse Pregnancy Outcomes

Recent research suggests a potential link between AP and adverse pregnancy outcomes(APOs), including preterm birth, low birth weight, and preeclampsia [40]. The inflammatory burden associated with AP may contribute to systemic inflammation and vascular dysfunction, increasing the risk of APOs. Understanding and addressing the oral health status of pregnant individuals, including the management of AP, may have implications for maternal and fetal health.

A systematic review evaluated the available evidence on the association between maternal AP and APOs. The review found a positive association between maternal AP and APOs, suggesting that the inflammatory mediators released in response to AP may contribute to systemic inflammation, a known risk factor for APOs. This inflammatory response triggered by AP could potentially affect pregnancy outcomes [40]. As the results of the little research in this area are inconclusive. Nevertheless, effectively managing oral health in pregnant individuals, including treating AP, may improve maternal and fetal health outcomes.

Autoimmune Disorders

Patients with autoimmune disorders such as rheumatoid arthritis or systemic lupus erythematosus may exhibit altered immune responses that affect the prevalence and outcomes of AP and RCT [41]. Dysregulated immune function in autoimmune disorders can influence the susceptibility to infections and the inflammatory response to microbial stimuli, potentially impacting the development and resolution of periapical lesions. Further research is needed to elucidate the specific mechanisms underlying the association between autoimmune disorders and periapical health.

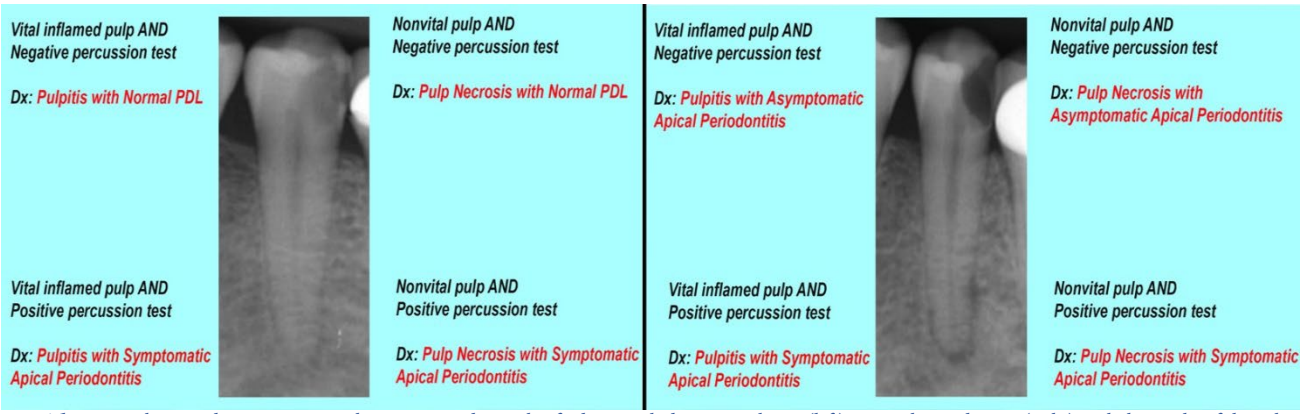

Figure 2. The comprehensive diagnostic approach integrates radiographic findings, including normal PDL (left) or apical periodontitis (right), with the results of clinical tests evaluating pulpal status and percussion sensitivity. This combined assessment enables the formulation of up to eight different clinical diagnoses (Dx).

Signs and Symptoms

AP manifests across a spectrum of clinical manifestations [42], ranging from mild discomfort to severe pain and swelling. Patients commonly report localized tenderness upon percussion, pain during biting or chewing, or the presence of a draining sinus tract. However, AP can also be asymptomatic (ALEO), emphasizing the importance of routine dental evaluations for early detection and intervention.

Radiographic Techniques in Dental Diagnosis

Conventional Techniques

Conventional radiographic techniques, including the bisecting angle and parallel techniques, are designed to minimize image distortion and improve diagnostic accuracy [43]. Taking multiple exposures from different angles can help prevent the overlap of structures, providing a clearer and more accurate depiction of periapical conditions. Based on the radiographic findings, such as the detection of periapical diseases (e.g., apical periodontitis) or the presence of a normal PDL, combined with the results of clinical tests assessing pulpal status and percussion sensitivity, up to eight different diagnoses can be made. This comprehensive approach is illustrated in Figure 2.

Advanced Imaging

These techniques offer a range of modalities to enhance the visualization of dental and periapical structures [43]. Panoramic radiography provides comprehensive views of the maxilla and mandible with improved quality and low radiation dose, while digital radiography reduces radiation exposure and offers immediate images, albeit with potentially lower spatial resolution. Subtraction radiography and densitometric analysis aid in detecting osseous changes over time, and magnetic resonance imaging (MRI) reveals soft tissue structures and inflammation, particularly beneficial in complex cases. Ultrasound assists in differentiating fluid, soft tissue, and blood flow, especially for lesions not covered by bone, while nuclear techniques offer high sensitivity for early detection of osseous lesions. Tomography and computer tomography (CT) provide detailed images, particularly useful in multirooted teeth, and cone-beam computed tomography (CBCT) is favored for detecting apical periodontitis due to its high-resolution 3D imaging capabilities and precise detection of lesion extension in the periapical area [44, 45]

Diagnostic Procedures

Diagnostic procedures for apical periodontitis involve a systematic approach encompassing history-taking, clinical examination, clinical tests, and radiographic examination [9]. Gathering medical and dental history, discussing symptoms, and evaluating previous treatments lay the foundation for a provisional diagnosis. Clinical examination, including extra-oral and intra-oral assessment, aids in identifying potential causative factors. Clinical tests such as pulp sensibility tests, percussion, mobility, and palpation refine the provisional diagnosis by assessing pulp and periapical status. Radiographic examination, utilizing periapical radiographs and CBCT, visualizes periapical changes and confirms the diagnosis.

It is important to note that while these tests are essential, they have limitations. For instance, a negative response to a sensitivity test does not always indicate necrotic pulp, as factors such as patient response variability, the type of test used, and the condition of the tooth can influence results. Therefore, the following taxonomy suggested here relies on a combination of clinical findings and radiographic evidence to provide a comprehensive assessment.

Integration of history, clinical, radiographic, and test findings is crucial for precise diagnosis and effective clinical management, considering the continuum of periapical disease stages.

Understanding these stages and utilizing a comprehensive taxonomy to classify clinical scenarios guides clinicians in tailoring therapeutic interventions for optimal treatment outcomes and long-term dental health (Table 1).

Treatment modalities

The treatment of teeth with carious lesions and/or pulp exposures can be categorized into four major scenarios based on the pulp status and clinical/radiographic findings:

Vital Tooth with Pulpal Inflammation, Negative Percussion Test, and No Radiographic Signs of PDL Widening (Diagnosis: Pulpitis)

For vital teeth exhibiting pulpal inflammation but lacking periapical involvement, treatment options primarily revolve around various VPTs, encompassing techniques such as pulp capping (both direct and indirect) and pulpotomy (miniature, partial, full). It should be noted that in situations where ALEOs are present without pulp exposure, non-aggressive DPC serves as a viable treatment approach. The fundamental goal of VPT is to sustain the vitality of the affected pulp by eliminating etiologic factors and filling/sealing the pulp chamber to prevent further microbial invasion. While RCT stands as an alternative option, it presents with increased intricacy and costliness. It is important to consider the impact of RCT on the levels of inflammatory mediators and overall health outcomes in cases of ALEOs. While the exact health benefits of RCT for ALEOs are still not fully understood, it is crucial to balance these potential benefits against the associated drawbacks. These drawbacks include the high cost of treatment, potential weakening of the tooth structure post-treatment, and the possibility of pain or discomfort following the procedure. Considering these factors, clinicians must carefully assess each individual case, taking into account the severity of symptoms, the extent of periapical pathology, and the patient's overall oral health status when determining the most appropriate treatment approach. Finally, health technology assessments (HTA) advocate for VPT in such scenarios, citing its less invasive nature, cost-effectiveness, and preservation of the natural tooth structure [46] (Figure 3).

Vital Tooth with Pulpal Inflammation, Positive Percussion Test, or Radiographic Signs of PDL Widening/Apical Lesion (Diagnosis: Pulpitis with AP)

In vital teeth where pulpal inflammation is accompanied by positive percussion test or radiographic evidence of PDL widening or apical lesions, the condition is diagnosed as pulpitis with AP. Similar to the previous scenario, VPTs and RCT are the primary treatment modalities. However, due to the presence of periapical pathology, RCT might be considered a more frequent treatment option based on outdated beliefs. Nonetheless, VPT remains a viable option (Figure 4) and is highly recommended by HTA for its cost-effectiveness and ability to maintain tooth vitality in such teeth [46-48]. But cases presenting symptomatic pulpitis concomitant with symptomatic AP probably warrant more aggressive intervention, such as full pulpotomy. The reported long-term success and survival rates for various VPTs for teeth diagnosed with pulpitis with or without apical periodontitis are 92% and 99%, respectively [49].

In endodontically treated teeth, ALEO in healthy patients requires monitoring to assess if the lesion progresses. This involves a "wait and watch" strategy, with the treatment decision made by considering whether to treat the lesion or observe it, with the patient involved in the decision-making. In vital teeth, the detection of AP, even when asymptomatic (ALEO), requires intervention to prevent potential complications.

Nonvital Tooth with Pulp Necrosis, Negative Percussion Test, and No Radiographic Signs of PDL Widening (Diagnosis: Pulp Necrosis)

For nonvital teeth with pulp necrosis but no periapical pathology, the recommended treatment is RCT. The objective

Table 1. Correlation of clinical signs and radiographic features with pulp status for accurate diagnosis of pulpal condition (i.e., pulpitis) and periapical status (i.e., apical periodontitis). This taxonomy aids in systematically classifying the different clinical scenarios encountered.

Pulp Condition	Clinical Sign (Percussion test)	Radiographic Sign	
		Normal PDL	PDL widening/Lesion
Vital	Negative	NP+NPDL	P+AAP
	Positive	P+SAP	P+SAP
Non-vital	Negative	PN+NPDL	PN+AAP
	Positive	PN+SAP	PN+SAP

NP: Normal Pulp, NPDL: Normal PDL, PN: Pulp Necrosis, P: Asymptomatic/symptomatic Pulpitis (It should be noted that the terms "reversible" and "irreversible" pulpitis should not be used further, as this misleading terminology should change due to the healing potential of pulps with a clinical diagnosis of irreversible pulpitis [50]), AAP: Asymptomatic Apical Periodontitis, SAP: Symptomatic Apical Periodontitis

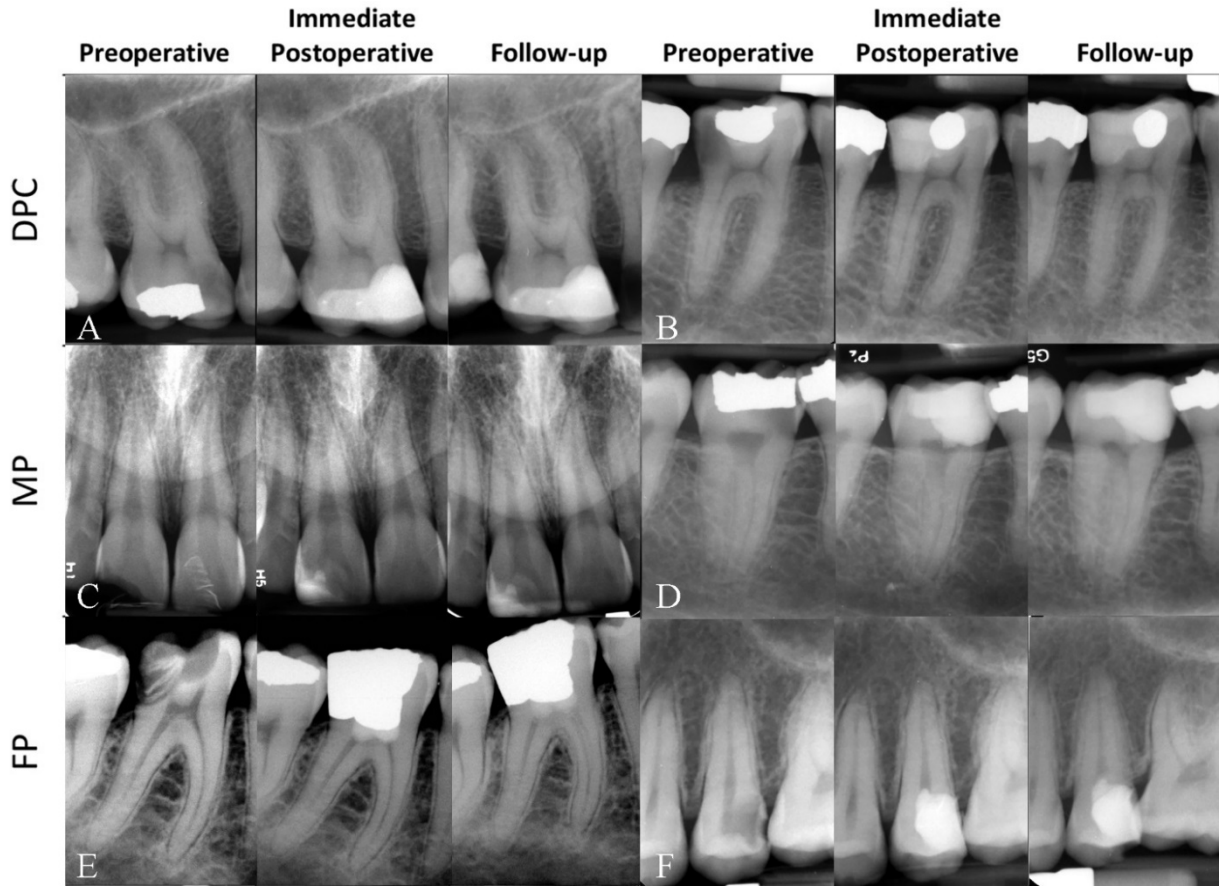

Figure 3. Successful cases illustrating various types of vital pulp therapy for teeth diagnosed with pulpitis but no apical periodontitis: A) Direct pulp capping of an upper right first molar in a 41-year-old female, with a 38-month follow-up demonstrating favorable treatment outcomes; B) Direct pulp capping of a lower first molar in a 35-year-old female, with a 24-month follow-up revealing dentin bridge formation and pulp preservation within the dentin boundary; C) Miniature pulpotomy performed on an upper central incisor following trauma and pulpal exposure in a 22-year-old male, with a 29-month follow-up showing successful results; D) Miniature pulpotomy of a lower second molar in a 28-year-old female, with a 42-month follow-up demonstrating dentin bridge formation and pulp preservation within the dentin boundary; E) Full pulpotomy of a lower first molar in a 26-year-old male, with a 39-month follow-up; F) Full pulpotomy of an upper second premolar in a 28-year-old male, with a 50-month follow-up revealing dentin bridge formation and pulp preservation within the dentin boundary.

of RCT in these cases is to remove the necrotic pulp tissue, disinfect the root canal system, and seal it to prevent reinfection. This treatment helps to restore the function of the tooth while eliminating any potential sources of infection.

Nonvital Tooth with Pulp Necrosis, Positive Percussion Test, or Radiographic Signs of PDL Widening (Diagnosis: Pulp Necrosis with AP)

In nonvital teeth where pulp necrosis is associated with positive percussion test or radiographic signs of PDL widening, the condition is diagnosed as pulp necrosis with AP. The treatment modality for such teeth is RCT, aimed at eradicating the infection, disinfecting the root canal system, and sealing it to prevent future microbial invasion. This approach is essential to resolve the periapical pathology and restore the functionality of involved tooth.

Future Directions in Research and Clinical Practice

Innovations in Diagnostic Technologies

Advancements in diagnostic technologies, such as high-resolution CBCT and advanced MRI, hold promise for providing more precise imaging of AP. These technologies offer improved detection of subtle pathological changes in AP, aiding in early and accurate diagnoses. Additionally, molecular diagnostics, including biomarkers and genetic profiling, show potential for early and specific identification of AP, which can significantly enhance treatment planning and outcomes.

Advances in Therapeutic Approaches

Therapeutic progressions aim to enhance the efficacy and predictability of endodontic treatments. Regenerative endodontics,

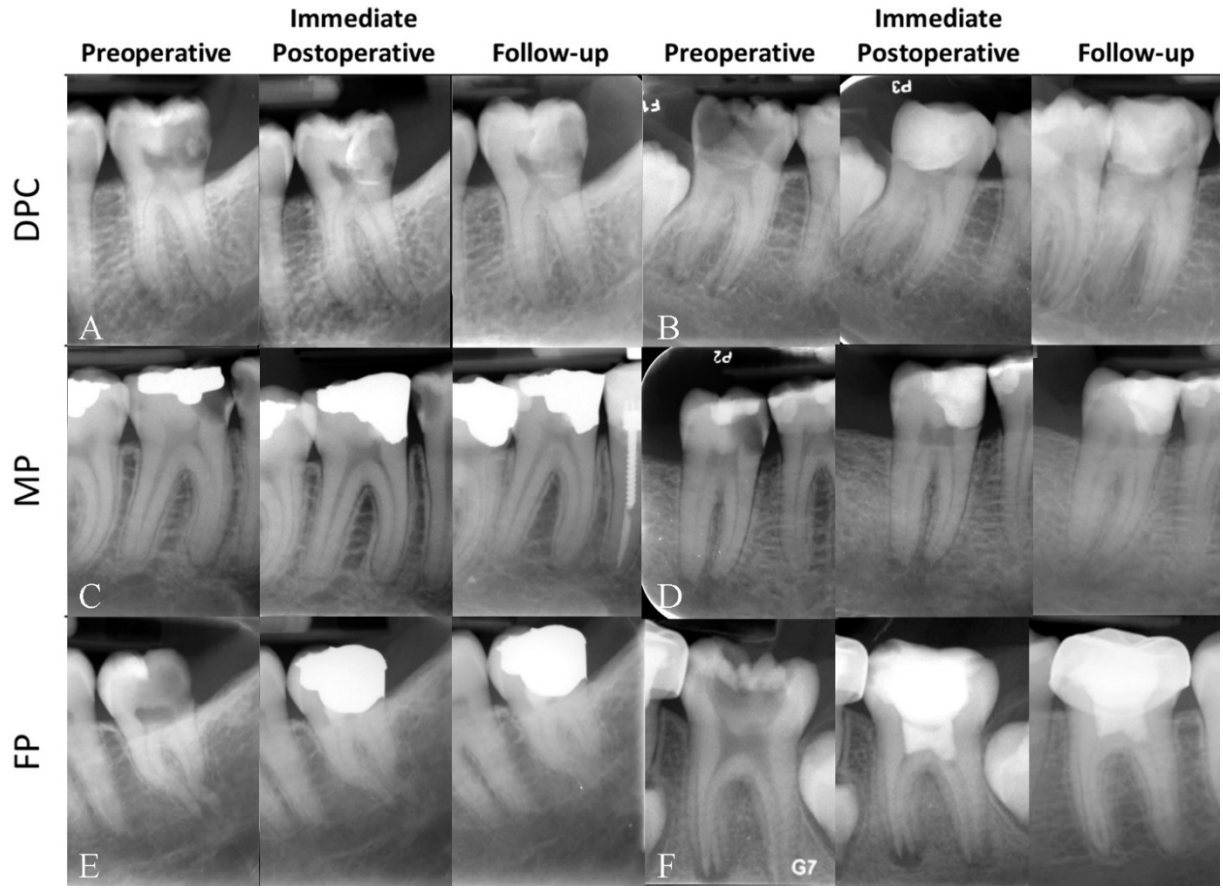

Figure 4. Illustrative cases showcasing various types of vital pulp therapy for teeth diagnosed with pulpitis associated with apical periodontitis: A) Direct pulp capping of a lower right second molar via a Class V cavity preparation in a 34-year-old male, with a 25-month follow-up demonstrating favorable treatment outcomes and a normal periodontal ligament (PDL); B) Direct pulp capping of a lower right second molar in a 16-year-old female, with a 62-month follow-up revealing preserved pulp and a normal PDL; C) Miniature pulpotomy performed on a lower right first molar in a 22-year-old male, with a 31-month follow-up showing dentin bridge formation, pulp preservation within the dentin boundary, and a normal PDL; D) Miniature pulpotomy of a lower second molar in a 41-year-old male, with a 52-month follow-up demonstrating dentin bridge formation, pulp preservation within the dentin boundary, and a normal PDL; E) Full pulpotomy of a lower third molar in a 47-year-old female, with a 46-month recall demonstrating favorable results and a normal PDL; F) Full pulpotomy of a lower left first molar in a 7-year-old female, with a 39-month recall revealing success attributed to root maturation and a normal PDL.

utilizing stem cell therapy and tissue engineering, present opportunities to restore damaged pulp-dentin complexes, promoting natural healing processes. Furthermore, nanotechnology applications, such as antimicrobial nanoparticles and nano-engineered materials, offer improved sealing and effectiveness in root canal treatments, potentially prolonging their durability and success rates.

Exploring Systemic Implications and Interventions

Research into the bidirectional relationship between AP and systemic health conditions, including diabetes and cardiovascular diseases, is paramount. Identifying biomarkers and inflammatory mediators linking oral and systemic health may lead to the development of novel therapeutic interventions targeting both AP and associated systemic conditions. Longitudinal studies are essential to comprehensively understand the long-term effects of AP and root canal treatments on systemic health, providing insights for tailored interventions and preventive strategies.

Directions for Longitudinal and Translational Research

Longitudinal studies tracking patients over time are crucial for identifying predictors of treatment success and failure in AP management. Translational research, which bridges basic science with clinical practice, holds promise for facilitating the development of new materials, technologies, and therapeutic strategies for widespread clinical application. Collaboration among researchers, clinicians, and industry stakeholders is pivotal for advancing the field of endodontics and improving patient outcomes.

Conclusion

Synthesis of Key Findings

This review provides a thorough examination of AP in both vital and nonvital teeth, delineating its clinical and radiographic features, underlying pathogenesis at cellular and molecular levels, epidemiology, and current diagnostic and therapeutic modalities. The intricate interplay between microbial factors and host responses underscores the complexity of AP development and progression, highlighting the need for precise diagnostic tools and effective treatments. In addition, the review emphasizes treatment strategies tailored specifically for teeth with pulp exposures, encompassing management approaches for pulpitis/AP.

Clinical and Public Health Implications

Timely detection and intervention are crucial in managing AP to mitigate its progression and associated complications. Advanced diagnostic technologies and therapeutic approaches show promise for significantly enhancing patient outcomes. Furthermore, the associations between AP and systemic health conditions underscore the importance of integrated healthcare approaches that consider the broader implications of dental infections on overall health.

Recommendations for Practice and Research

In clinical practice, the adoption of advanced diagnostic and therapeutic technologies is recommended to improve the accuracy and efficacy of AP management. Continuous education and training for dental professionals on the latest advancements in endodontics are essential. For research endeavors, further exploration into the pathogenesis of AP, its systemic implications, and the development of innovative treatments should be prioritized. Collaborative, interdisciplinary research efforts are indispensable for translating scientific discoveries into clinical practice, ultimately enhancing patient care and public health outcomes.

Acknowledgements

NA

Conflict of interest

None.

Funding support

NA

Author contributions

Saeed Asgary: Conceptualization, Writing the Original Draft, Review/Editing, and Visualization. Anita Aminoshariae: Cowriting the Original Draft, Review/Editing. Paul R Wesselink: Cowriting the Original Draft, Review/Editing.

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Please cite this paper as: Asgary S, Aminoshariae A, Wesselink PR. Apical Periodontitis in Vital and Nonvital Teeth: Clinical and Radiographic Features. Iran Endod J. 2024;19(3): 148-57. *Doi: 10.22037/iej.v19i3.45605.*