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ORIGINAL ARTICLE

Relationship between inflammation site and apical periodontitis in patients with severe endodontic pain

ABSTRACT

Aim: *To assess the relationship between inflammation site and apical periodontitis in patients with severe endodontic pain on periapical radiographs using a periapical index (PAI) scoring system.*

Methodology: *This was a retrospective study of patients who visited the Department of Endodontics, Faculty of Dentistry, X University between January 2020 and December 2021 with the complaint of severe endodontic pain. After application of specific exclusion criteria, 985 patients with severe endodontic pain were included. Inflammation in the patient population was classified as follows: a positive response to the electric pulp test (stage 1), a negative response to the electric pulp test without swelling (stage 2) or a negative response to the electric pulp test with swelling (stage 3). Using the PAI scoring system, periapical status was then classified as healthy (PAI: 1 or 2) or unhealthy (PAI: 3, 4 or 5). The level of significance was set at 5% (*$p<0.05$*).*

Results: *The lowest severity of apical periodontitis (AP) was found in patients with a positive response to the electric pulp test (stage 1) (*$p<0.05$*). Among cases with a negative response to the electric pulp test, the incidence of AP was significantly higher in patients with swelling than in those without swelling (*$p<0.05$*).*

Conclusions: *The present study detected a relationship between the main site of inflammation and AP in patients with severe endodontic pain. The presence or absence of AP might serve as a useful indicator in patients with severe endotontic pain.*

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Introduction

A proper endodontic diagnosis is essential to guide appropriate treatment. In the past, histological, clinical and radiographic findings were used to guide the diagnosis. However, the relationship between these findings and tooth status was not always clear (1, 2). In recent years, to improve the endodontic diagnostic approach and overcome diagnostic difficulties due to dilemmas, dental anamnesis and clinical and radiographic evidence have been used (3, 4). As endodontic infections arise in the pulpal space and then spread to the periapex (5), endodontic diagnosis depends on pulp vitality, percussion sensitivity and palpation tests, which are used to determine the status of periapical tissues (3). The endodontic diagnosis is relatively uncomplicated in patients who present with severe pain or spontaneous pain. However, the histological and clinical evidence may be inconclusive in patients who present without pain (6-8).

Thus far, no studies have investigated periapical radiographic findings in endodontic patients with severe pain. From a clinical perspective, this might appear insignificant, as root canal treatment is indicated in such conditions, whether bone resorption is detected on a periapical radiograph or not. However, it is important to clarify this relationship to identify the source of pain and origin of endodontic infection. Due to the way in which teeth and surrounding tissue is encoded by the sensory nervous system, inflammation of various structures (i.e., pulp, periodontal ligament, or periosteum) can cause pain (9).

Periapical radiographs are routinely used to examine healing progress in endodontically treated teeth using a periapical index (PAI) scoring system (10). This scoring system was developed based on histological and radiographic examinations of teeth in human cadavers (11, 12). Using the PAI scoring system, inflammation is assessed on a scale of 1-5, where 1 denotes no inflammation and 5 denotes severe inflammation. As the PAI scoring system is based on cadaver studies, whether the examined teeth were symptomatic or not at the moment of death is unclear. In addition, these studies did not address superimposition related to posterior teeth. An additional weakness of the PAI scoring system is its dependence on visible evidence from images of inflammation stages as they appear on periapical radiographs (11-13).

In the last decade, the use of cone-beam computed tomography (CBCT) in endodontic diagnosis has increased. However, CBCT is not routinely used to aid endodontic diagnoses due to its high radiation dose (14, 15). Furthermore, previous research demonstrated that periapical inflammation identified by CBCT may be temporary, even in cases of a high level of inflammation (16). In addition, a study focusing on RANKL/osteoprotegerin and interleukin-8 in pulpal and periapical pathology pointed out that bone resorption takes precedence over inflammation (17). On the other hand, such differences related to highly inflamed pulps were not investigated on periapical radiographs, although the opinion that small periapical lesions cannot be identified in posterior teeth has been disputed (18-20).

Given the importance of periapical radiographs in endodontic diagnosis, it is important that they shed light on bone inflammation. Unexpectedly, there seems to be an absence of information correlating severe pain and inflammation in endodontic patients based on periapical radiographs. Thus, the aim of the present study was to correlate inflammation (stage) with periapical status (healthy or unhealthy) in patients who presented to our department with severe endodontic pain using periapical radiographs and the PAI index.

Materials and Methods

Study design

The present study was approved by the ethics committee of X University (2022/66-17) and performed in accordance with the Declaration of Helsinki. The records of patients who visited the Department of

Endodontics, Faculty of dentistry, X University between January 2020 and December 2021 with severe endodontic pain were examined retrospectively. At the time of presentation, the patients were questioned about primary problems and symptoms. All the patients then underwent a complete endodontic evaluation by the endodontist on duty at the time. The examiners who performed during the evaluation had been calibrated.

Exclusion criteria
The exclusion criteria included pregnancy, immunosuppressive drug taking, long-term use of anti-inflammatory drugs and antibiotics use over the previous month. In addition, to ensure that only patients with severe pain of endodontic origin were included, all patients with a Visual Analogue Scale (VAS) score of <7 were excluded. Additional exclusion criteria were commencement of endodontic treatment for the patient's complaint at another institution or failure to make an accurate diagnosis. Finally, periapical radiographs with artefacts and of poor quality were excluded.

Clinical and radiographic assessment
The patients scored the highest pain level experienced in the previous 24 hours on the VAS, where a VAS score of 0 denoted "no pain" and a score of 10 denoted "the worst pain imaginable" (21). The patients were also asked about the pain duration of the affected teeth, including whether they had experienced spontaneous pain for more than 1 week. Inspection of the affected tooth and surrounding tissues, an electric pulp test and a percussion sensitivity test were performed for clinical examination. The affected tooth was compared to the contralateral tooth, which was free of pain and swelling. The dental history of each patient was documented in a chart. Periapical radiographs were taken using a phosphor plate radiography system (Dürr Dental, Bietigheim-Bissingen, Germany) with a film holder, using the parallel technique for standardization.
In the retrospective evaluation, one experienced endodontist assessed the radiographs using Picture Archiving and Communication Systems software version (1.1.1.6) for Windows 10 (Microsoft Corporation, Redmont, WA, U.S.A.), with the images displayed on a 28-inch Samsung LU28H750UQMXUF (Samsung Electronics, Seoul, South Korea) at a 3,840×2,160 pixel resolution.

Data collection
Patient age and sex, pain duration (<1 week and >1 week), sensitivity to percussion, location (maxilla or mandible), tooth type (incisor, canine, premolar, or molar), presence and type of restoration (composite, amalgam, crown, or bridge abutment), presence of root canal filling, response to the pulp vitality test (positive or negative) and presence of swelling were recorded in a specially designed form.

Assessment of periapical status
Periapical status was assessed radiographically using the 5-point scale of the PAI scoring system to determine the presence of periapical pathology (12). For calibration, two endodontists with at least 5 years of experience examined 50 periapical radiographs. Disagreement between the examiners was resolved through discussion until consensus was reached. The calibration was performed twice, with a 1-week interval. Intra- and interexaminer consensus were then calculated using Cohen's kappa coefficient. For intraexaminer consensus, the values were 0.79 and 0.76, and the value for interexaminer consensus was 0.71, suggesting substantial agreement (22). Both endodontists then assessed the periapical radiographs under standard conditions. In cases of uncertainty, the higher PAI score was selected. For multirooted teeth, the highest PAI score assigned to individual roots was used. During the evaluation, the examiners were blinded to both patient- and tooth-related information.

Statistical analysis
For statistical analysis, inflammation was classified as positive response to the electric pulp test (stage 1), negative response

to the electric pulp test without swelling (stage 2) or negative response to the electric pulp test with swelling (stage 3), and periapical status (healthy=PAI of 1 or 2; unhealthy=PAI of 3, 4 or 5). IBM SPSS Statistics for Windows, version 22 (IBM Corp., Armonk, NY, U.S.A.) was used for statistical analysis of the findings. A chi-square test was used to compare qualitative data. Descriptive data are presented as mean, standard deviation and frequency. The level of significance was set at 5% ($p< 0.05$).

Results

Demographic data

Between January 2020 and December 2021, 2,051 patients visited the Department of Endodontics, Faculty of Dentistry, X University with severe endodontic pain. After elimination of patients according to the exclusion criteria, 985 patients were included in the study. The mean age of the patients was 32.9±12.8 years. The male:female ratio was 40.9:59.1%.

Evaluation of clinical status

The incidence of stage 2 inflammation was significantly higher than stage 1 or 3 inflammation. In addition, the incidence of stage 1 was significantly higher than stage 3 (Table 1).

In terms of pain history, it was significantly longer in the stage 1 group than stage 2 and stage 3 groups ($p<0.05$). Percussion sensitivity was significantly lower in the stage 1 group as compared with that in the other groups ($p<0.05$). The percentage of incisors and restored teeth was significantly lower in the stage 1 group as compared with that in the other groups ($p<0.05$). The percentage of canines in the stage 3 group was significantly higher than that in the other groups ($p<0.05$), whereas the percentage of molars in the stage 1 group was significantly higher compared to that in the other groups ($p<0.05$). In the stage 3 group, the incidence of endodontically treated teeth was significantly higher in comparison with that in the stage 2 group ($p<0.05$) (Table 2).

Correlation between clinical status and AP

A correlation was detected between the main site of inflammation and pain severity. In this study, a PAI score of 3 or higher denoted AP. The incidence of AP was lowest in the stage 1 group (pulpal inflammation) ($p<0.05$). The incidence of AP was significantly higher in the stage 3 group than that in the stage 2 group ($p<0.05$) (Table 2).

Further evaluation of AP

Neither age nor sex was statistically significantly associated with the presence of AP. The incidence of AP was significantly higher in patients with pain histories of more than 1 week and sensitivity to percussion ($p<0.05$). Teeth located in the mandible also had higher percentages of AP ($p<0.05$). Furthermore, incisors showed a statistically higher presence of AP than other tooth types ($p<0.05$). The incidence of AP in endodontically treated teeth in the stage 3 group was significantly higher than that in the stage 2 group ($p<0.05$) (Table 3).

Table 1
Evaluation of clinical status

	Subject	
	n	%
Stage 1	381	38.7
Stage 2	526	53.4
Stage 3	78	7.9
p	0.000*	

One sample chi-square test **p<0.05*

Discussion

The present study on patients who presented to our department with severe endodontic pain showed that inflammation was correlated with AP based on a retrospective evaluation of periapical radiographs, PAI scores and clinical status.

PAI scores projected the process of inflammation from the pulp to the periodontal ligament and later periapex. Furthermore, PAI scores of the teeth were not significantly affected by anatomical structures.

Table 2
Evaluations of case groups

		Stage 1	Stage 2	Stage 3	p
		n (%)	n (%)	n (%)	
Age	13-19	89 (23.4)	102 (19.4)	22 (28.2)	0.002*
	20-29	88 (23.1)	112 (21.3)	16 (20.5)	
	30-39	111 (29.1)	138 (26.2)	12 (15.4)	
	40-49	69 (18.1)	100 (19)	14 (17.9)	
	50-59	17 (4.5)	37 (7)	10 (12.8)	
	60+	7 (1.8)	37 (7)	4 (5.1)	
Sex	Male	162 (42.5)	215 (40.9)	26 (33.3)	0.323
	Female	219 (57.5)	311 (59.1)	52 (66.7)	
Duration of pain	<1 week	110 (28.9)	298 (56.7)	53 (67.9)	0.000*
	>1 week	271 (71.1)	228 (43.3)	25 (32.1)	
Percussion sensitivity	Absent	99 (26)	100 (19)	9 (11.5)	0.004*
	Present	282 (74)	426 (81)	69 (88.5)	
Jaw	Maxilla	186 (48.8)	274 (52.1)	37 (47.4)	0.534
	Mandible	195 (51.2)	252 (47.9)	41 (52.6)	
Tooth type	Incisor	11 (2.9)	41 (7.8)	9 (11.5)	0.000*
	Canine	12 (3.1)	20 (3.8)	7 (9)	
	Premolar	75 (19.7)	107 (20.3)	23 (29.5)	
	Molar	283 (74.3)	358 (68.1)	39 (50)	
Restoration	None	273 (71.7)	250 (47.5)	33 (42.3)	0.000*
	Composite	68 (17.8)	131 (24.9)	27 (34.6)	
	Amalgam	40 (10.5)	102 (19.4)	9 (11.5)	
	Crown	0 (0)	16 (3)	2 (2.6)	
	Bridge abutment	0 (0)	27 (5.1)	7 (9)	
Root canal filling	Absent	381 (100)	423 (80.4)	51 (65.4)	0.000*
	Present	0 (0)	103 (19.6)	27 (34.6)	
AP	Absent	368 (96.6)	338 (64.3)	10 (12.8)	0.000*
	Present	13 (3.4)	188 (35.7)	68 (87.2)	

*Chi-square test *p<0.05*

In addition, most of the patients with negative responses to the electric pulp test who had severe endodontic pain did not show evidence of AP at the time of the evaluation.

Despite a lack of certainty in endodontic diagnosis in patients presenting with tooth pain, inflammation can be classified as follows: stage 1, severely painful inflammation of the pulp; stage 2, severe tooth pain with necrotizing or necrotic pulp; and stage 3, severe periapical pain with swelling. The decision to perform root canal treatment is based on both a clinical and radiographic examination.

Considering the routine use of digital periapical radiography, it is surprising that there have been no systematic studies of periapical radiographic images obtained from patients with severe endodontic pain. The present study aimed to shed light on this subject. No histological or CBCT examination results exist to confirm our findings. As this was a retrospective study, a histological examination was not practicable. Furthermore, to prevent unnecessary exposure to radiation, CBCT was not performed in cases of severe endodontic pain where the cause of the pain could be clearly diagnosed

In accordance with similar studies in the literature (23, 24), the incidence of a negative response to the vitality test was significantly higher in patients than in those with a positive response to the vitality test. The patients in the present study were selected from those who attended a university hospital. The socioeconomic status of the patients who attend such hospitals, which provide free or low-cost care, tends to be relatively low, and the patients tend to neglect dental care needs. The aforementioned may explain the high incidence of necrotic pulp cases in the present study. Rechenberg et al. found that teeth in stage 1 group were less restored (24). In this study, the restored teeth in this case group were significantly lower than in the other groups.

This finding is also likely due to neglect of dental care, with the patients not consulting a dental practitioner until they experienced severe pain. Failure to seek

Table 3

Evaluations regarding the presence of AP

		Without AP	With AP	p
		n (%)	n (%)	
Age	13-19	152 (71.4)	61 (28.6)	0.095
	20-29	158 (73.1)	58 (26.9)	
	30-39	201 (77)	60 (23)	
	40-49	135 (73.8)	48 (26.2)	
	50-59	38 (59.4)	26 (40.6)	
	60+	32 (66.7)	16 (33.3)	
Sex	Male	285 (70.7)	118 (29.3)	0.248
	Female	431 (74.1)	151 (25.9)	
Duration of pain	<1 week	298 (64.6)	163 (35.4)	0.000*
	>1 week	418 (79.8)	106 (20.2)	
Percussion sensitivity	Absent	164 (78.8)	44 (21.2)	0.025*
	Present	552 (71)	225 (29)	
Jaw	Maxilla	377 (75.9)	120 (24.1)	0.024*
	Mandible	339 (69.5)	149 (30.5)	
Tooth type	Incisor	33 (54.1)	28 (45.9)	0.000*
	Canine	25 (64.1)	14 (35.9)	
	Premolar	140 (68.3)	65 (31.7)	
	Molar	518 (76.2)	162 (23.8)	
Restoration (n=429)	Composite	136 (60.2)	90 (39.8)	0.108
	Amalgam	107 (70.9)	44 (29.1)	
	Crown	9 (50)	9 (50)	
	Bridge abutment	21 (61.8)	13 (38.2)	
Root canal filling (n=604)	Absent	672 (78.6)	183 (21.4)	0.000*
	Present	44 (33.8)	86 (66.2)	

Chi-sqare test **p<0.05*

prompt tooth restoration treatment for primary caries lesions led to severe inflammation and pain.

A comprehensive systematic review of the literature may clarify and aid clinicians in performing an optimal root canal treatment (25). On the other hand, pain may be considered as a pre-operative diagnostic criterion as well as a treatment success parameter (26). In the present study, the percentage of patients in the stage 1 group with a pain history of more than 1 week was significantly higher than that in the other groups. Rechenberg et al. presented a similar result (24). This finding can be explained by inflammation not yet reaching the periapical tissues. Thus, a pain history of 1 week or longer may be seen in patients with stage 1 inflammation.

Pulpal inflammation may give rise to severe pain, emergency visits to dental clinics and systemic symptoms (23, 24, 27). The diagnoses in the present cases were uncomplicated, with progression of pulpal inflammation, as demonstrated by a positive response to the electric pulp test, to inflammation affecting the periodontium and then periapical tissue. Many of the patients in the present study showed tenderness to percussion. Based on the terminology of the American Association of Endodontists, the endodontic diagnosis in these cases may have been symptomatic AP.

In this context, it is natural that the percentage of percussion sensitivity was significantly lower in the group with a positive response in the electric pulp test than that in the other groups and significantly higher when AP was present compared to when AP was absent.

In the present study, AP more commonly affected the mandible than maxilla. Among tooth types, molars were least affected by AP. In contrast, Rechenberg et al. found no significant difference in AP according to tooth type (24). Differences in the study population, dental care habits and assessment methods may explain the discord between the results of the two studies.

Of note, in this study, 38.6% of patients with a negative response to the electric pulp test showed no signs of AP (PAI score <3). The most probable reason for this finding is lesion dynamics. In addition, most of the patients with a negative response to the electric pulp test in the present study declared that the pain duration was less than 1 week. The presence of AP may explain the pain duration in these patients.

In the present study, the periapical radiographic images showed the primary site of inflammation in patients with severe endodontic pain. In most cases, inflammation and severe pain showed rapid onset, with no history of periapical lesions. In our study, the incidence of endodontically

treated teeth and that of AP were low. This finding is in line with that of studies reporting that severe pain in the presence of persistent AP is rare (24, 28).
On the other hand, Rechenberg et al. reported a relatively high incidence of AP in endodontically treated (root-filled) teeth, as reflected by higher PAI scores (24).
Similarly, the presence of AP was more common among endodontically treated teeth in this study.
Factors that can lead to AP include untreated root canals, inadequate root canal obturation and iatrogenic procedural errors. An endodontic infection, whether symptomatic or asymptomatic, is affected by the number and virulence of microorganisms and the state of the immune system (29).
Rechenberg et al. reported that periapical inflammation accompanied by severe pain may be associated with the volume of root canal accessible to microorganisms (24). This may explain why the percentage of endodontically treated teeth was low in the present study. However, it should be acknowledged that the cause of severe endodontic pain remains unexplained in most cases. Further studies are needed to shed light on this subject, as it is a significant part of clinical endodontics.

Conclusions

The present study detected a relationship between the main site of inflammation and AP in patients with severe endodontic pain. As compared with patients with a negative response to the electric pulp test, those with a positive response to the electric pulp test were characterized by a pain history of more than 1 week, less percussion sensitivity, less number of dental restorations and less presence of AP. AP was associated with a pain history of less than 1 week, percussion sensitivity, mandibles, endodontic treatment and a negative response to the electric pulp test.
Considering these findings, the presence or absence of AP might be a useful indicator of endodontic diagnosis in patients with severe endodontic pain.

Clinical Relevance

To provide information about the relationship between the inflammation and the periapical status, as it is an important part of endodontics and as there is an absence of information correlating severe pain and inflammation in endodontic patients based on periapical radiographs.

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Conflict of Interest

The authors declare no conflict of interest.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

References

1 *Baume LJ. Dental pulp conditions in relation to carious lesions. Int Dent J. 1970;20:309–337.*
2 *Dummer PM, Hicks R, Huws D. Clinical signs and symptoms in pulp disease. Int Endod J. 1980;13:27–35.*
3 *American Association of Endodontists. AAE consensus conference recommended diagnostic terminology. J Endod. 2009;35:1634.*
4 *Glickman GN (2009) AAE consensus conference on diagnostic terminology: background and perspectives. J Endod. 2009;35:1619–1620.*
5 *Langeland K. Tissue response to dental caries. Endod Dental Traumatol. 1987;3:149–171.*
6 *Hasler JE, Mitchell DF. Painless pulpitis. J Am Dent Assoc. 1970;81:671–677.*
7 *McCarthy PJ, McClanahan S, Hodges J, Bowles WR. Frequency of localization of the painful tooth by patients presenting for an endodontic emergency. J Endod. 2010;36:801–805.*
8 *Ricucci D, Loghin S, Siqueira JFJ. Correlation between clinical and histologic pulp diagnoses. J Endod. 2014;40:1932–1939.*
9 *Byers MR, Narhi MV. Dental injury models: experi-€ mental tools for understanding neuroinflammatory interactions and polymodal nociceptor functions. Crit Rev in Oral Biol Med. 1999;10:4–39.*
10 *Ørstavik D. Time-course and risk analyses of the*

development and healing of chronic apical periodontitis in man. Int Endod J. 1996;29:150–155.
11 Brynolf I. A histological and roentgenological study of the periapical region of human upper incisors. 1967 Stockholm: Almqvist & Wiksell.
12 Ørstavik D, Kerekes K, Eriksen HM. The periapical index: a scoring system for radiographic assessment of apical periodontitis. Endod Dental Traumatol. 1986;2:20–34.
13 Cheung GS, Wei WL, McGrath C. Agreement between periapical radiographs and cone-beam computed tomography for assessment of periapical status of root filled molar teeth. Int Endod J. 2013;46:889–895.
14 Pauwels R, Beinsberger J, Collaert B et al. Effective dose range for dental cone beam computed tomography scanners. Eur J Radiol. 2012;81:267–271.
15 ESE developed by: Patel S, Brown J, Semper M, Abella F, Mannocci F. European Society of Endodontology position statement: use of cone beam computed tomography in Endodontics: European Society of Endodontology (ESE) developed by. Int Endod J. 2019;52:1675–1678.
16 Hashem D, Mannocci F, Patel S et al. Clinical and radiographic assessment of the efficacy of calcium silicate indirect pulp capping: a randomized controlled clinical trial. J Dent Res. 2015;94:562–568.
17 Rechenberg DK, Bostanci N, Zehnder M, Belibasakis GN. Periapical fluid RANKL and IL-8 are differentially regulated in pulpitis and apical periodontitis. Cytokine. 2014;69:116–119.
18 Bender IB, Seltzer S. Roentgenographic and direct observation of experimental lesions in bone: I. J Am Dent Assoc. 1961a;62:152–160.
19 Bender IB, Seltzer S. Roentgenographic and direct observation of experimental lesions in bone: II. J Am Dent Assoc. 1961b;62:708–716.
20 Chang L, Umorin M, Augsburger RA, Glickman GN, Jalali P. Periradicular lesions in cancellous bone can be detected radiographically. J Endod. 2020;46:496–501.
21 Sadaf D, Ahmad MZ. Factors associated with postoperative pain in endodontic therapy. Int J Biomed Sci. 2014;10:243-247.
22 Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics. 1977;33:159–174.
23 Rechenberg DK, Held U, Burgstaller JM, Bosch G, Attin T. Pain levels and typical symptoms of acute endodontic infections: a prospective, observational study. BMC Oral Health. 2016;16:61.
24 Rechenberg DK, Munir A, Zehnder M. Correlation between the clinically diagnosed inflammatory process and periapical index scores in severely painful endodontically involved teeth. Int Endod J. 2021;54:172-180.
25 Nobar BR, Dianat O, Nobar BR et al. Effect of rotary and reciprocating instrumentation motions on postoperative pain incidence in non-surgical endodontic treatments: A systematic review and meta-analysis. Eur Endod J. 2021;6(1):3-14.
26 Iaculli F, Rodriguez-Lozano FJ, Briseno-Marroquin B, Wolf TG, Spagnuolo G, Rengo S. Vital pulp therapy of permanent teeth with reversible or irreversible pulpitis: An overview of the literature. J Clin Med. 2022;11(14):4016.
27 Nalliah RP, Allareddy V, Elangovan S et al. Hospital