CLINICAL RESEARCH

The Effect of Systemic Statin Intake on Healing of Apical Periodontitis after Nonsurgical Root Canal Treatment: A Retrospective Cohort Study

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SIGNIFICANCE

Increasing the knowledge about the influence of some medications, such as statins, and the healing of apical periodontitis is a topic that is becoming increasingly important in recent literature, as endodontic diseases are increasingly no longer considered just a clinical dental disease but rather highly correlated to the general health of the individual considered.

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ABSTRACT

Introduction: This retrospective cohort study compared the radiographic healing of apical periodontitis following root canal treatments and retreatments in patients regularly taking statins versus those who had never taken statins. **Methods:** Patients who underwent root canal treatment or retreatment performed by undergraduate and postgraduate students were included. The patients were divided into 2 age-matched groups: those who reported regularly taking statins and those who had never taken statins. The outcome was assessed using periapical radiographs taken at least at 1-year post-treatment. Teeth with short root canal fillings were excluded. Single and multiple binary logistic regression tested the association between statin use and radiographic treatment outcome while adjusting for root-canal and restoration quality, diabetes mellitus, cardiovascular diseases, patient age, tooth type, and follow-up period. **Results:** A total of 122 teeth were analyzed: 62 from patients taking statins and 60 from patients not taking statins. Using lenient criteria, logistic regression showed no significant difference in healing rates between the statin and control groups (90.3% vs. 90%; OR = 1.04; P = .952). However, under strict criteria, patients taking statins had a significantly lower probability of success compared to controls (62.9% vs 85%; OR = 0.30; P = .008). **Conclusions:** Patients taking statins had a lower number of radiographic complete healings than those not taking statins. The results of this study challenge the presumed benefits of systemic statins intake on AP healing. *(J Endod 2025;51:1384–1392.)*

KEY WORDS

Apical periodontitis; healing; immune response; root-canal treatment; Statins

Apical periodontitis (AP) is a chronic inflammatory condition caused by the immune system's reaction to persistent microbial infection within the root canal system of an affected tooth[1]. It is characterized by destruction of periradicular tissues due to etiologic agents of endodontic origin [2], which can lead to tissue breakdown and bone resorption.

Nonsurgical root canal treatment (NSRCT) with adequate chemo-mechanical disinfection and homogeneous obturation is the standard treatment for AP. The primary objective is to reduce the microbial load within the root canal system, thereby promoting healing of the periapical tissues by providing a favorable environment for tissue repair[3]. After the initial endodontic treatment, radiographic assessments using periapical radiographs have shown healing in approximately 78-92% of teeth[4], with up to 95% of treated teeth remaining asymptomatic and functional[5]. However, the success rate of NSRCT is significantly lower when a preoperative periapical radiolucency is present.

While the main cause of NSRCT failure is the presence of bacteria within the root canal space, delayed healing may also be linked to the host immune system and its impaired reparative response[6]. Furthermore, systemic diseases can delay periapical healing by affecting bone turnover, fibroblast function, and microvascular activity; thereby diminishing nutrient and oxygen supply to the periapical region and promoting the persistence of granulomatous tissue[7].

Several studies have suggested that adjunct pharmacological therapy, whether locally administered as intracanal medications[8] or systemically[9], may potentially enhance the healing of apical periodontitis. In particular, regular statin intake has been linked to improved AP healing[10].

Statins are well-tolerated drugs used to lower high cholesterol by inhibiting 3-hyroxy-3-methylglutaryl-coenzyme A reductase. By inhibiting key rate-limiting enzymes in the mevalonate pathway, statins exhibit a broader spectrum of action, termed pleiotropic effects[11]. Apart from their lowering cholesterol properties, statins have also demonstrated antimicrobial, anti-inflammatory, and pro-osteogenic properties[12]. Statins enhance osteoblast differentiation, up-regulate vascular endothelial growth factor and bone morphogenetic protein and suppress both bone resorption and osteoclast formation[13].

There is limited literature exploring the association between statins and healing of AP following endodontic therapy. Therefore, the objective of this retrospective cohort study was to assess the association between statin intake and the radiographic healing of AP by comparing the success rates of nonsurgical root canal treatments (NSRCT) and retreatments in patients with at least one year of post-treatment follow-up periapical radiographs, to those of patients who had never taken statins. Several other variables potentially associated with treatment outcomes were also considered. The null hypothesis was that the percentage of healing/healed teeth after root canal treatments and retreatments does not significantly differ between patients taking statins and those not taking statins.

MATERIALS AND METHODS

Ethical approval was obtained before the commencement of this study from Guy's and St Thomas' Hospital (Electronic Record Research Interface (GERRI) IRAS ID: 257283 Rec Reference: 20/EM/0112 extension granted 28/11/2023). The study adhered to the STROBE checklist for retrospective cohort studies (Supplementary Table 1).

Patient Selection

Retrospective data were compiled by screening the accessible dental and medical records of all patients who sought endodontic evaluation and care between 2009 and 2021. Specifically, data were collected from patients who underwent NSRCT or retreatment with at least one-year follow-up periapical radiographs. Treatments were performed by undergraduate students or postgraduate residents.

Patient Data Extraction

We used the "Salud Report Query Builder" software (Two-Ten Health, Dublin, Ireland) to anonymously identify subjects based on predefined inclusion and exclusion criteria (Table 1). Patients with root canal fillings more than 2 mm short of the radiographic apex were excluded. Data collected included patient age, medical history questionnaire responses, root canal treatment procedure codes, and confirmation of follow-up periapical radiographs. To assemble the study group meeting the inclusion criteria, anonymized periapical radiographs were reviewed and examined using "Planmeca Romexis Dental Imaging Software" (Planmeca, Helsinki, Finland). The collected data were then consolidated for analysis.

Study Variables

The primary focus of this research was the radiographic healing outcome following NSRCT or retreatment. Additionally, several other variables were considered, including patient demographics (age, gender), presence and size of periapical radiolucency, type of statin intake, tooth type and position (anterior, premolar, molar), procedure type (primary treatment or retreatment), medical history, treatment outcome, operator qualification (undergraduate or postgraduate), root filling quality, smoking status, types of coronal restoration (plastic restorations, crowns/onlays), quality of the coronal seal, and ethnicity. All these factors were treated as independent variables potentially influencing the radiographic healing outcomes.

Data Collection Methods

Patient medical and dental history information was obtained from electronic records using the "Salud software" (Two-Ten Health Limited) through a completed questionnaire.

Radiographic Assessment

All periapical radiographs were examined and viewed using the Planmeca Romexis dental imaging software (Planmeca; Helsinki, Finland) displayed on a 15-inch HP monitor. To ensure consistency, contrast and brightness settings were kept uniform throughout the evaluation. The assessment was performed by two calibrated examiners: one endodontist and one final-year postgraduate endodontic student. Both examiners were blinded to the group allocation during outcome assessment.

For calibration, the examiners independently identified the presence or absence of AP in 50 teeth from periapical radiographs that were not part of this study. Each examiner then reassessed the same 50 teeth after 4 weeks to check interexaminer reliability. In cases of disagreement, the less favorable score was selected.

Additionally, the longest diameter of the periapical radiolucency was measured. The radiographic healing outcome was evaluated using the classification system by Patel et al[14] using "lenient" and "strict" criteria as described in Table 2.

Information was recorded regarding the presence of periapical lesions and any increase or decrease in their size, as well as the quality and length of root canal fillings and the type and quality of coronal restorations. Root canal fillings were considered of good quality if radiographs showed a tapered, dense obturation extending within 0.5 to 2 mm of the radiographic apex in all observable canals[15]. Restorations were classified as defective if a visible gap was present between the tooth and the restoration on recall radiographs.

Teeth with root canal fillings more than 2 mm short of the radiographic apex were excluded.

Sample Size

The sample included 122 teeth from 108 patients, divided into 2 age-matched groups: the statin group (62 teeth) and the control group (60 teeth) (Fig. 1).

Data Management and Statistical Analysis

The collected data were anonymized before being transferred to an Excel spreadsheet. Subsequently, a comparison was made between patients taking statins and those in the control group. Statistical analyses were conducted using IBM SPSS (version 23) (Armonk, NY, USA). Categorical variables were described using absolute and relative frequencies, while continuous variables were summarized by mean, standard deviation, range, median, and quartiles for both the total sample and by group.

At the patient level, Chi^2, independent t-test, and Mann–Whitneyś tests were performed to assess group homogeneity. Each patient contributed 1, 2, or 3 teeth to the analysis.

At the tooth level, tests of homogeneity were also conducted. Multilevel simple logistic regressions using generalized estimation equations were used to assess the probability of success per tooth by group and other variables. Raw odds ratios (ORs) were estimated. Variables with *P* values less than 0.1 were included in the final multiple

TABLE 1 - Inclusion and Exclusion Criteria for Study and Control Groups

Study group	Control group
Inclusion criteria	
• Males and females >35 y. • Confirmed intake of systemic statins during endodontic assessment and follow-up. • Teeth with favorable periodontal condition with no more than 5 mm loss of attachment. • Preoperative, postoperative, and 1-y or more follow-up periapical radiographs, that showing the entire tooth from crown to 4 mm beyond apex. • Anterior, premolar and molar teeth.	• Males and females >35 y. • No intake of statins. • Teeth with favorable periodontal condition with no more than 5 mm loss of attachment. • Preoperative, postoperative, and minimum 1-y follow-up periapical radiographs, that showing the entire tooth from crown to 4 mm beyond apex.
Exclusion criteria	
• Patients < 35 years of age. • Patients taking bisphosphonates hormone replacement therapy, antiresorptive treatment, discontinued statins > 1 year before follow-up. • Patients with poor, unclear, or missing clinical notes. • Teeth with unfavourable periodontal condition (>5 mm attach. loss). • Root apices not discernible in periapical radiograph. • Root canal fillings short of radiographic apex by more than 2 mm.	• Patients < 35 years of age. • Patient with poor, unclear, or missing clinical documentation. • Root apices not discernible in periapical radiograph. • Root canal fillings short of radiographic apex by more than 2 mm. • Patients taking, hormone replacement therapy, bisphosphonates, antiresorptive treatment.

regression models to obtain adjusted ORs and 95% confidence intervals based on Wald's Chi-square statistic. The significance level was set at 5% ($\alpha = 0.05$).

A prior power analysis was performed based on Alghofaily et al[10], who reported healing rates of 93% and 70% in patients taking statins versus those not taking statins, respectively. For this effect size, it was calculated that a minimum of 95 patients (or 95 independent teeth, one tooth per patient) would be needed to achieve 80% power. However, since some patients in our study provided more than one tooth, the power level was adjusted according to the two-level data structure. Assuming that 20% of patients would provide more than one tooth and a within-subject correlation of CCI = 0.8, a correction coefficient of D = 1.16 was applied. Therefore, a minimum of 110 dependent teeth were required to achieve 80% power under the same conditions.

RESULTS

This retrospective study analyzed 122 teeth from 108 patients, divided into a statin group (62 teeth) and a control group (60 teeth). Overall, 56 participants were male (51.9%) and 52 were female (48.1%), with a mean age of 61.7 ± 10.5 years, ranging from 37 to 87 years. The smoking rate was 10.2%. Fifty-four participants with 60 teeth were included in the control group, while 54 participants with 62 teeth were enrolled in the statin group. No significant differences were observed between the groups regarding age, gender, smoking status, presence of AP, or years of follow-up. Ten teeth (5 per group) received root canal retreatments; all other teeth received primary treatments. The prevalence of preoperative periapical lesions at tooth level was 62.3%. All primary treatments were undertaken on nonvital teeth. Fifty-one teeth had been symptomatic preoperatively—23 in the statin group and 28 in the control group.

Diabetes mellitus prevalence in the statin group was 37.1% at the tooth level (23 teeth in 20 patients). Different types of statin medications were taken by patients, particularly Simvastatin and Atorvastatin. Each patient provided one, two or three teeth. The mean largest diameter of periapical radiolucencies was 5.7 mm in the statin group and 5.9 mm in the control group. The mean recall rate for the studied participants was 3.4 years, while the median recall rate was 3 years. The distribution in the statin and control groups of the independent variables potentially associated with the radiographic healing of the treatment is shown in Table 3.

All root canal treatments were performed using rubber dam isolation. All periapical radiographs were taken using the paralleling technique, and working lengths were established with an apex locator. Postgraduate students used an operative microscope; clinical instructors supervising undergraduate students also used the operative microscope. Both postgraduate and undergraduate students treated molar teeth, but endodontic retreatments were performed only by postgraduate students.

There were only 3 cases in which minor extrusion of root filling material was observed—2 in the control group and one in the statin group. All 3 teeth showed evidence of radiographic healing.

In the statin group, 8 patients were taking steroids (see Supplementary Table 2): three via inhalers and five orally. Of these cases, 3 teeth showed complete resolution of the radiolucency, 2 had no radiolucency at either baseline or recall, 2 showed no reduction in the size of the radiolucency, and one showed a reduction. In the control group, there was only one patient using steroids, and this patient did not have any radiolucency at baseline or recall.

At the tooth level, variables such as procedure type (primary root canal treatment vs. retreatment), operator qualification

TABLE 2 - Outcome of Root Canal Treatment by Groups

Outcome categories for root canal (re) treatment		Group		
Score	Outcome	Total, N (%)	Control, N (%)	Statins, N (%)
1	New periapical radiolucency	1 (0.8)	1 (1.7)	0 (0.0)
2	Enlarged periapical radiolucency	5 (4.1)	2 (3.3)	3 (4.8)
3	Unchanged periapical radiolucency	6 (4.9)	3 (5.0)	3 (4.8)
4	Reduced periapical radiolucency	20 (16.4)	3 (5.0)	17 (27.4)
5	Resolved periapical radiolucency	46 (37.7)	27 (45.0)	19 (30.6)
6	Unchanged healthy periapical status [no radiolucency before and after root canal (re)treatment].	44 (36.1)	24 (40.0)	20 (32.3)

'Healing' outcome (lenient criterion): Success-healing[4-6] vs failure[1-3].
'Healed' outcome (strict criterion): Success-healed[5,6] vs failure[1-4].

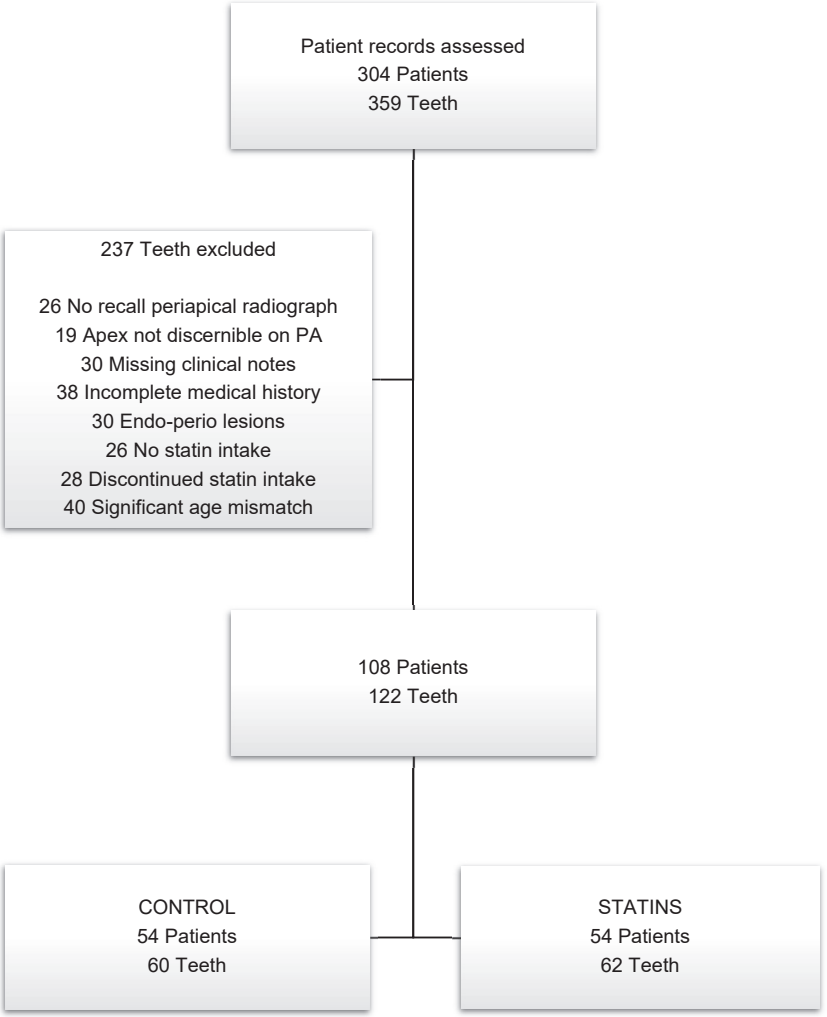

FIGURE 1 – Total number of patients and teeth in control and study group "patients taking statins (ST)". AP, apical periodontitis.

(undergraduates vs. postgraduates), root canal filling quality, presence of coronal coverage, and quality of coronal restoration were similar between the groups. However, the percentage of molars differed, representing 43.5% of treated teeth in the statin group compared to 66.7% in the control group ($P = .019$). The clinical notes indicated that only 2 teeth—one from the statin group and one from the control group—exhibited symptoms of acute apical periodontitis at recall. Both teeth showed radiographic evidence of an increase in the size of the radiolucency present at baseline. All other teeth were functional, not tender to percussion or palpation, and clinical examination revealed unremarkable surrounding tissues.

Effect of Statins on the Outcome of RCT

Using a simple binary regression model with lenient criteria, the probability of radiographic healing did not differ between groups (OR = 1.04; $P = .952$), with radiographic healing rates of 90.0% in the control group and 90.3% in the statin group. The presence of voids within the obturation was associated with a significant reduction of the radiographic healing (OR = 0.09; $P = .024$). No other factors showed significant associations with the radiographic healing outcome.

The multiple regression model with lenient criteria included tooth type and AP presence as confounders and confirmed no significant group difference ($P = .529$). Voids in obturation remained the only significant factor ($P = .030$) (Table 4).

However, when strict criteria were applied using a simple regression model, differences emerged. The statin group had a significantly lower complete radiographic healing rate (62.9%) compared to controls (85.0%) (OR = 0.30; $P = .008$). Teeth with AP showed a markedly reduced probability of radiographic complete healing (OR = 0.03; $P = .001$). Longer follow-up periods correlated with higher radiographic healing probability (OR = 1.34; $P = .007$).

Further analysis using strict criteria in a multiple regression model, which included AP and recall duration as potential confounding factors, showed that the probability of complete radiographic healing was significantly reduced in patients receiving statins (OR = 0.31; $P = .044$). Additionally, teeth affected by AP demonstrated a lower probability of healing compared to those without AP (OR = 0.03; $P = .001$), and longer follow-up periods were associated with a higher probability of complete radiographic healing (OR = 1.36; $P = .054$) (Fig. 2).

DISCUSSION

In this retrospective study, the investigation into the radiographic healing of AP following NSRCT and retreatment, and its correlation with systemic statin intake, revealed that using lenient success criteria, statin intake did not yield significant differences in AP radiographic healing compared to the control group. However, under strict criteria, the statin group demonstrated less radiographic healing compared to the control group. Both findings challenge the presumed benefits of statins in supporting AP healing[10,16].

The observation that statin intake may limit the progression and aid the healing of apical periodontitis is primarily based, to the author's knowledge, on a few animal studies[17,18] and one retrospective human cohort study[10]. Compared to Alghofaily et al[10], this study included a larger sample (122 vs 60 teeth) with similar follow-up durations, and critically, age matching between statin and control groups, whereas the previous study's statin group was significantly older. These methodological differences may explain the substantial disparities in the findings and account for the radically different results.

In animal studies, statins predominantly showed a protective effect against bone loss triggered by the inflammatory mechanisms of AP[18,19], achieved by reducing the expressions of factors essential for bone resorption[20]. The results of such studies were represented by a greater reduction in the size of experimentally induced periapical radiolucencies following RCT, or by a reduced size of the radiolucencies created by the experimentally induced root canal infections[17].

However, it is essential to acknowledge that the results of these animal studies, where AP is experimentally induced by triggering a short-term inflammatory response, might differ from those in human AP. In humans, the

TABLE 3 - Descriptive Statistics of the Sample at the Tooth Level

	Group		
	Total, N (%)	**Control, N (%)**	**Statins, N (%)**
	122 (100)	**60 (49.2%)**	**62 (50.8)**
Gender			
Male	63 (51.6)	28 (46.7)	35 (56.5)
Female	59 (48.4)	32 (53.3)	27 (43.5)
Age			
Mean ± Standard deviation	61.7 ± 10.5	61.5 ± 10.2	61.9 ± 10.9
Smoking			
No	109 (89.3)	56 (93.3)	53 (85.5)
Yes	13 (10.7)	4 (6.7)	9 (14.5)
Disease			
None			28 (45.2)
DM			23 (37.1)
CVS			10 (16.1)
Prevalence of AP			
No	46 (37.7)	25 (41.7)	21 (33.9)
Yes	76 (62.3)	35 (58.3)	41 (66.1)
Drug			
Simvastatin			22 (35.5)
Atorvastatin			27 (43.5)
Other			13 (21.0)
follow up Mean ± Standard deviation	3.4 ± 2.3	3.7 ± 2.7	3.1 ± 1.7
Tooth Type			
Anterior	18 (14.8)	4 (6.7)	14 (22.6)
Premolar	37 (30.3)	16 (26.7)	21 (33.9)
Molar	67 (54.9)	40 (66.7)	27 (43.5)
Procedure			
RCT	112 (91.8)	55 (91.7)	57 (91.9)
Re-RCT	10 (8.2)	5 (8.3)	5 (8.1)
Undergraduate	89 (73.0)	43 (71.7)	46 (74.2)
Postgraduate	33 (27.0)	17 (28.3)	16 (25.8)
Quality			
No voids	118 (96.7)	59 (98.3)	59 (95.2)
Voids	4 (3.3)	1 (1.7)	3 (4.8)
Cuspal Coverage			
No	21 (17.2)	8 (13.3)	13 (21.0)
Yes	91 (74.6)	49 (81.7)	42 (67.7)
Coronal Restoration			
Good	96 (78.7)	48 (80.0)	48 (77.4)
Defective	26 (21.3)	12 (20.0)	14 (22.6)

AP, apical periodontitis; CVS, cardiovascular system; RCT, root canal treatment.

infection causing the inflammatory response leading to periapical bone loss is relatively long-standing and persistent. Therefore, the effect of statins on the healing of AP in humans after RCT might not be similar to the outcomes observed in these animal studies.

None of the animal studies investigated the proportion of complete healing following NSRCT. Simvastatin was shown to have the ability to reduce Cyr61 synthesis in osteoblasts, consequently inhibiting the progression of experimentally induced apical periodontitis in rats, which in turn led to diminished macrophage infiltration[17]. Macrophages, critical innate immune cells, are responsible for recognizing and eliminating exogenous pathogens in microbe-mediated infectious diseases. When periapical tissues are challenged by bacterial invasion, the resident macrophages may respond to foreign material, such as bacteria and their toxin, thereby regulating both physiological and pathologic processes[21].

It is possible that the anti-inflammatory effects of statins may initially reduce bone resorption, leading to a decreased size of apical radiolucencies in the short term. However, persistent interference with the inflammatory process[17] may potentially result in a longer-term impairment of the immune response to bacterial penetration into the periapical tissues. This could reduce the number of complete radiographic healings.

Within the statin group, diabetic patients exhibited similar radiographic healing of periapical radiolucencies compared to nondiabetic patients (87.5% vs 92.1% under lenient criteria; 62.5% vs 63.2% under strict criteria). The differences did not reach statistical significance, probably due to the small number of diabetic patients (23 patients). Systematic reviews and meta-analyses have indicated a higher prevalence of AP and periapical radiolucencies in diabetic patients[22], along with the presence of larger periapical osteolytic lesions[23]. The prognosis for root-filled teeth was observed to be worse in diabetic individuals[24]. Furthermore, nondiabetic patients within the statin group in this study showed a significantly lower number of complete healings than patients in the control group (63.2% vs 85.0%). This provides additional support to the hypothesis that statins independently reduce the probability of complete healing of AP after NSRCT or retreatment.

The role of IGF-1 in bone formation has been extensively studied, with numerous studies highlighting its importance in regulating osteoblast differentiation and proliferation, as well as promoting bone development and homeostasis[25,26]. A systematic review has noted that hormones like IGF-1 play a crucial role in bone formation and in mitigating bone diseases such as periodontitis[27]. Additionally, research has shown that IGF-1, when combined with other growth factors, can enhance bone formation around dental implants in rabbits[28,29].

Studies have also found that statins can negatively impact IGF-1 levels[30,31]. These findings may help explain the impaired bone healing observed in this study, particularly among diabetic patients taking statins.

Both groups included patients who were taking various antihypertensive medications and medications for other conditions such as proton pump inhibitors and anticoagulants. As expected, the number of such patients was higher in the statin group, which also included diabetic patients. All teeth in both groups exhibited adequate length of root canal fillings. Moreover, there was no difference between the 2 groups in terms of operator experience, the number of primary treatments and retreatments, and the number of preoperative periapical radiolucencies. In conclusion, the 2 groups were as homogeneous as possible in terms of factors potentially associated with the radiographic healing of endodontic treatments, considering the nature of the study.

The study has several limitations. Its retrospective design inherently restricted the scope of analysis. Reliance on historical

TABLE 4 - Success (Lenient Criteria) by Independent Factors: Results of Simple and Multiple Binary Logistic Regression using GEE (Raw and Adjusted Odds Ratios, 95% CI)

Model type	Variables	Total, N (%)	Success, N (%)	OR	95% CI	*P* value
Simple binary logistic regression	Group	122 (100)	110 (90.2)	1 1.04	0.31 – 3.43	.952
	Control	60 (100)	54 (90.0)			
	ST	62 (100)	56 (90.3)			
	Gender				0.19 – 2.15	.471
	Male	63 (100.0)	58 (92.1)	1		
	Female	59 (100.0)	52 (88.1)	0.64		
	Age					
	Mean ± Standard deviation	61.7 ± 10.5	61.5 ± 10.2	0.98	0.91 – 1.05	.590
	Smoking					
	No	109 (100)	98 (89.9)	1		
	Yes	13 (100)	12 (92.3)	1.35	0.15 – 11.8	.788
	Ethnicity					
	White	31 (100)	27 (87.1)	1		
	Non-White	23 (100)	21 (91.3)	1.56	0.25 – 9.58	.634
	Disease					
	None	28 (100)	25 (89.3)	1		.603
	DM	23 (100)	20 (87.0)	0.80	0.14 – 4.54	.801
	CVS	10 (100)	10 (100)	—	—	—
	Prevalence of AP					
	No	46 (100)	45 (97.8)	1		
	Yes	76 (100)	65 (85.5)	0.13	0.02 – 1.06	.057
	Drug					
	Simvastatin	22 (100)	19 (86.4)	1		.750
	Atorvastatin	27 (100)	25 (92.6)	1.97	0.29 – 13.4	.487
	Other	13 (100)	12 (92.3)	1.90	0.17 – 20.9	.602
	Follow up Mean ± Standard deviation	3.4 ± 2.3	3.5 ± 2.3	1.24	0.87 – 1.78	.235
	Tooth Type					
	Anterior	18 (100)	15 (83.3)	1		.248
	Premolar	37 (100)	36 (97.3)	7.20	0.69 – 75.0	.099
	Molar	67 (100)	59 (88.1)	1.48	0.35 – 6.22	.597
	Procedure					
	RCT	112 (100)	101 (90.2)	1		
	Re-RCT	10 (100)	9 (90.0)	0.98	0.11 – 8.86	.986
	Undergraduate	89 (100)	80 (89.9)	1		
	Postgraduate	33 (100)	30 (90.9)	1.13	0.28 – 4.48	.867
	Quality					
	No voids	118 (100)	108 (91.5)	1		
	Voids	4 (100)	2 (50.0)	0.09	0.01 – 0.73	**.024***
	Cuspal Coverage					
	No	21 (100)	20 (95.2)	1		
	Yes	91 (100)	81 (89.0)	0.41	0.05 – 3.37	.405
	Coronal Restoration					
	Good	96 (100)	85 (88.5)	1		
	Defective	26 (100)	25 (96.2)	3.24	0.40 – 26.5	.274
Multiple binary logistic regression	Group					
	Control			1		
	ST			1.63	0.35 – 7.54	.529
	Prevalence of AP					
	No			1		
	Yes			0.12	0.01 – 1.08	.058
	Tooth Type					
	Anterior			1		.311
	Premolar			6.15	0.56 – 67.9	.138
	Molar			1.47	0.22 – 9.77	.691
	Quality					
	No voids			1		
	Voids			0.11	0.01 – 0.81	**.030***

AP, apical periodontitis; CVS, cardiovascular system; DM, diabetes mellitus; GEE, generalized estimation equations; RCT, root canal treatment.
*$P < .05$. **$P < .01$. ***$P < .001$.
Bold values indicate statistical significance.

Model type	Variables	Total, N (%)	Success, N (%)	OR	95% CI	p-value
Simple binary logistic regression	GROUP	122 (100)	90 (73.8)			
	Control	60 (100)	51 (85.0)	1		
	ST	62 (100)	39 (62.9)	0.26	0.11 – 0.62	**0.002****
	GENDER					
	Male	63 (100.0)	45 (71.4)	1		
	Female	59 (100.0)	45 (76.3)	1.29	0.55 – 2.99	0.560
	AGE			1.00	0.96 – 1.05	0.983
	Mean ± Standard deviation	61.7±10.5	61.7±10.0			
	SMOKING					
	No	109 (100)	83 (76.1)	1		
	Yes	13 (100)	7 (53.8)	0.37	0.09 – 1.51	0.165
	ETHNICITY					
	White	31 (100)	20 (64.5)	1		
	Non-White	23 (100)	14 (60.9)	0.86	0.26 – 2.81	0.797
	DISEASE					0.481
	None	28 (100)	16 (57.1)	1		
	DM	23 (100)	14 (60.9)	1.17	0.37 – 3.71	0.794
	CVS	10 (100)	8 (80.0)	3.00	0.50 – 18.1	0.230
	PREVALENCE OF AP					
	No	46 (100)	45 (97.8)	1		
	Yes	76 (100)	45 (59.2)	0.03	0.01 – 0.25	**0.001****
	DRUG					0.483
	Simvastatin	22 (100)	14 (63.6)	1		
	Atorvastatin	27 (100)	15 (55.6)	0.71	0.22 – 2.29	0.571
	Other	13 (100)	10 (76.92)	1.91	0.42 – 8.65	0.404
	FOLLOW UP			1.34	1.08 – 1.65	**0.007****
	Mean ± Standard deviation	3.4±2.3	3.7±2.4			
	TOOTH TYPE					0.065
	Anterior	18 (100)	9 (50.0)	1		
	Premolar	37 (100)	30 (81.1)	4.29	1.19– 15.4	**0.026***
	Molar	67 (100)	51(76.1)	3.19	1.07 – 9.51	**0.038***
	PROCEDURE					
	RCT	112 (100)	83 (74.1)	1		
	Re-RCT	10 (100)	7 (70.0)	0.82	0.18 – 3.78	0.794
	Undergraduate	89 (100)	67 (75.3)	1		
	Postgraduate	33 (100)	23 (69.7)	0.76	0.32 – 1.78	0.520
	QUALITY					
	No voids	118 (100)	88 (74.6)	1		
	Voids	4 (100)	2 (50.0)	0.34	0.05 – 2.54	0.294
	CUSPAL COVERAGE					
	No	21 (100)	16 (76.2)	1		
	Yes	91 (100)	68 (74.7)	0.92	0.33 – 2.56	0.879
	CORONAL RESTORATION					
	Good	96 (100)	72 (75.0)	1		
	Defective	26 (100)	18 (69.2)	0.75	0.28 – 2.02	0.569
Multiple binary logistic regression	GROUP					
	Control			1		
	ST			0.31	0.09 – 0.97	**0.044***
	PREVALENCE OF AP					
	No			1		
	Yes			0.03	0.01 – 0.25	**0.001****
	FOLLOW UP			1.36	0.99 – 1.85	0.054
	TOOTH TYPE					0.407
	Anterior			1		
	Premolar			2.87	0.55 – 14.9	0.210
	Molar			1.81	0.36 – 9.16	0.471

FIGURE 2 – Success (strict criteria) by independent factors: Results of simple and multiple binary logistic regression using GEE. GEE, generalized estimation equations.

medical and dental records may have led to missing or incomplete data on important variables, such as the nature of patient-reported symptoms and diabetic status (well-controlled vs uncontrolled). The statin-naöve control group included patients with varying health conditions and polypharmacy, limiting more detailed analysis of statin use and healing. Notably, 8 patients in the statin group used steroids—either inhaled or oral—which have been linked to impaired healing of apical periodontitis; however, only 3 of these teeth failed to heal.

Despite these limitations, the correlations observed suggest that statin use may serve as a potential flag for identifying patients at risk of delayed radiographic healing. Radiographic evaluation relied on periapical radiographs, which have known limitations in detecting periapical lesions[32]. Finally, variability and lack of detailed data on statin dosage and duration introduce potential confounding factors that may have influenced the results.

CONCLUSION

The results of this study showcased that, in comparison to patients who were not taking statins, patients on statins had a lower number of complete radiographic healings of apical periodontitis following nonsurgical root canal treatments and retreatments. Further research, including prospective trials is necessary to understand the potential impact of statins on periapical healing.

CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

Esha Goel: Methodology, Data curation, Formal analysis, Investigation, Project administration, Validation, Writing – original draft, Writing – review & editing. **Shahrah Mkhreb:** Data curation, Validation, Writing – review & editing. **Elisabetta Cotti:** Methodology, Writing – review & editing. **Francesca Ideo:** Methodology, Writing – review & editing. **Sadia Niazi:** Methodology, Data curation, Formal analysis, Investigation, Project administration, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. **Garrit Koller:** Conceptualization, Methodology, Formal analysis, Validation, Writing – review & editing. **Samira Farzadi:** Data curation, Methodology, Writing – review & editing. **Francesco Mannocci:** Conceptualization, Methodology, Formal analysis, Validation, Writing – review & editing.

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SUPPLEMENTARY MATERIAL

Supplementary material associated with this article can be found in the online version at www.jendodon.com (https://doi.org/10.1016/j.joen.2025.06.010).

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