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Apicoectomy versus apical curettage in combination with or without L-PRF application: a randomized clinical trial

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This study compared the efficacy of apicoectomy and apical curettage with and without leukocyte- and platelet-rich fibrin (L-PRF) in treating large periapical lesions. Sixty-four adults (30 male, 34 female) with a previously endodontically treated tooth and a large periapical lesion were randomized into four groups (n = 16): retrograde obturation (RG), orthograde obturation (OG), RG + L-PRF, and OG + L-PRF. All participants underwent root canal retreatment in two sessions. The RG group underwent root-end resection and retrograde MTA obturation, the RG + L-PRF group underwent L-PRF application to the bone defect following the RG protocol, the OG group underwent orthograde MTA obturation and periapical curettage without root-end resection, and the OG + L-PRF group underwent L-PRF application following the OG protocol. Clinical and radiographic assessments were performed preoperatively, and at 1 week and 1, 3, 6, 9, and 12 months postoperatively. At follow-up visits, pain scores, swelling, tooth mobility, tenderness to percussion (T-PER), tenderness to palpation (T-PAL), and the presence of fistula were clinically assessed. Periapical radiography determined the periapical index (PAI) score and measured the periapical lesion area (PALA). The Kruskal–Wallis test was performed to test the effect of a single independent variable (factor) on a dependent variable. No statistically significant differences were identified between the groups for preoperative PAI scores, pain scores, swelling, tooth mobility, fistula, T-PER, or T-PAL ($p > 0.05$). At postoperative week 1, the RG + L-PRF group showed a significantly lower T-PER. The RG + L-PRF group showed significantly lower PALA values and significantly higher PALA healing rates at postoperative 1, 6, and 9 months. Both L-PRF groups achieved PALA healing rates of over 90% at 9 months. It was concluded that a combination of apicoectomy and L-PRF effectively treats periapical lesions and promotes both short- and long-term healing and that a combination of periapical curettage and L-PRF offers a less invasive alternative, especially when the crown-to-root ratio is a concern.

Trial registration: The protocol was registered at ClinicalTrials.gov (NCT05847647).

Keywords Apical curettage, Apicoectomy, Bone regeneration, Leucocyte- and platelet-rich fibrin, Mineral trioxide aggregate, Ortograde obturation, Periapical lesion, Retrograde obturation, Root-end resection

Despite improvements in endodontic treatment, persistent or recurrent apical periodontitis (AP) remains a problem. AP may develop after endodontic treatments, thereby requiring additional procedures, such as nonsurgical retreatment or periapical surgery. A variety of challenges associated with retreatment, including the difficulty of removing previous obturation materials, may threaten the success of retreatment and necessitate surgical intervention[1].

Apicoectomy is a common periapical surgical procedure that involves curettage of the inflammatory periapical tissue and resection of the apical portion of the root. Many studies have recognized apicoectomy as an important part of periapical surgical procedures and a prerequisite for treatment success[2], but it has some risks. Roots that have already weakened and thinned due to periodontitis increase their susceptibility to fracture by resection. In addition, especially in cases in which the ratio between the crown and root length is impaired, the stability of the restoration is adversely affected, and the stability of the tooth in the socket may become questionable in the long term[3]. In such cases, less invasive techniques, such as periapical curettage without root-

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end resection, may be a more conservative treatment option. In the literature, few case reports have described the clinical success of periapical surgery performed with periapical curettage without root-end resection[4–8]. However, to our knowledge, no controlled clinical trials have investigated the effect of periapical curettage on periapical healing in apical periodontitis.

The primary goal of apical surgery is to create an optimal environment for periradicular tissue healing by eliminating the source of infection. However, in certain situations, such as large apical lesions, through-and-through lesions, and apicomarginal lesions, the success of apical surgery may be compromised. Various biomaterials, including bone substitutes, barrier membranes, growth factors, autologous platelet concentrates, or a combination of these agents, have been used in apical surgery to enhance periapical healing by stimulating cell differentiation, proliferation, induction, and conduction of tissue formation[9]. Among these biomaterials, autologous platelet concentrates have gained significant interest due to their autologous nature, ease of preparation, and rich content of growth factors.

Platelet concentrates derived from autologous blood centrifugation have undergone significant advancements over time. First-generation products, such as growth factor–rich plasma and platelet-rich plasma (PRP), laid the groundwork for the development of second-generation products, such as pure platelet-rich fibrin (PRF), leukocyte- and platelet-rich fibrin (L-PRF), advanced platelet-rich fibrin (A-PRF), and injectable platelet-rich fibrin (i-PRF). L-PRF was first developed by Choukroun et al. for use in oral and maxillofacial surgery and has shown good potential as a biomaterial. It is defined as a strong fibrin matrix with biomechanical properties in which platelets, leukocytes, and cytokines are trapped and released after a certain period[10]. Current studies evaluating the effects of various PRF preparations on tissue regeneration have reported positive contributions to hard and soft tissue healing in regenerative dental applications, including implant therapy, periodontal procedures, and alveolar and gingival augmentation techniques[11,12].

Clinical studies evaluating the effect of PRF on radiographic and clinical healing in periapical surgical procedures have yielded variable results due to differences in PRF preparation protocols, the design of the intervention groups, periapical lesion sizes, follow-up periods, and radiographic and clinical evaluation methods; some studies reported significant improvements[13–18], while others reported no significant effect on healing[19,20]. These controversies emphasize the need for further research. In light of the above information, the present study aimed to assess the clinical efficacy of periapical curettage and apicoectomy procedures in combination with the use of L-PRF in the management of teeth with large periapical lesions. The null hypothesis of this study is that the apical curettage technique performed without root-end resection provides clinical and radiological results comparable to the root-end resection technique in the treatment of teeth with large periapical lesions.

Materials and methods

Study design and patient selection

This single-center, prospective, randomized, controlled clinical trial was conducted at the Departments of Endodontics and Oral and Maxillofacial Surgery in the Faculty of Dentistry at Istanbul Medipol University. The study protocol was approved by the Ministry of Health's Clinical Research Ethics Committee (approval no: 567333164-203-E.5273, dated 10/10/2019). The protocol was registered at www.clinicaltrials.gov and the registration number is NCT05847647 (06/05/2023). The study followed the CONSORT guidelines (2010) and was conducted in accordance with the World Medical Association's Declaration of Helsinki. All patients were informed regarding the benefits and risks, as well as alternative treatment choices, before enrollment in the trial, and written informed consent was provided.

According to the a priori power analysis of a study[21] conducted to investigate the effect of periapical lesion size on healing results after regenerative endodontic procedures using preoperative and postoperative periapical lesion volume data (G*Power 3.1.9.4 software, Franz Faul, Germany), it was calculated that there should be at least three samples from each dependent group to conduct a similar study (effect size 3.39, $\alpha = 0.05$, power = 0.80). However, in the present study, groups of 16 subjects each were planned to achieve a stronger statistical prediction. Therefore, 64 adult volunteers (30 males, 34 females) were selected from 1100 patients who presented to the Department of Endodontics with apical periodontitis between February 2022 and March 2023. Details on participant enrollment, randomization, allocation, intervention completion, and analysis are presented in a CONSORT flow diagram (Fig. 1).

The inclusion criteria included the following:

- Presence of a previously endodontically treated single-rooted tooth with a single root canal and a periapical lesion 5–12 mm in diameter.
- A periapical index (PAI) score of 4 or 5[22].

The exclusion criteria included the following:

- Pregnancy or lactation.
- Systemic disease or medication use that may affect wound healing or contraindicate oral surgery (e.g., radiotherapy, chemotherapy, corticosteroid use, antiplatelet/anticoagulant therapy, connective tissue disease, vascular disease, blood dyscrasia, liver disease, diabetes).
- Smoking more than 10 cigarettes per day.
- Endodontic treatment within the last 2 years.
- Previous periapical surgery on the same tooth.
- Periodontal disease (pocket depth > 4 mm).
- Incomplete root development.
- Traumatic occlusion or excessive coronal destruction.

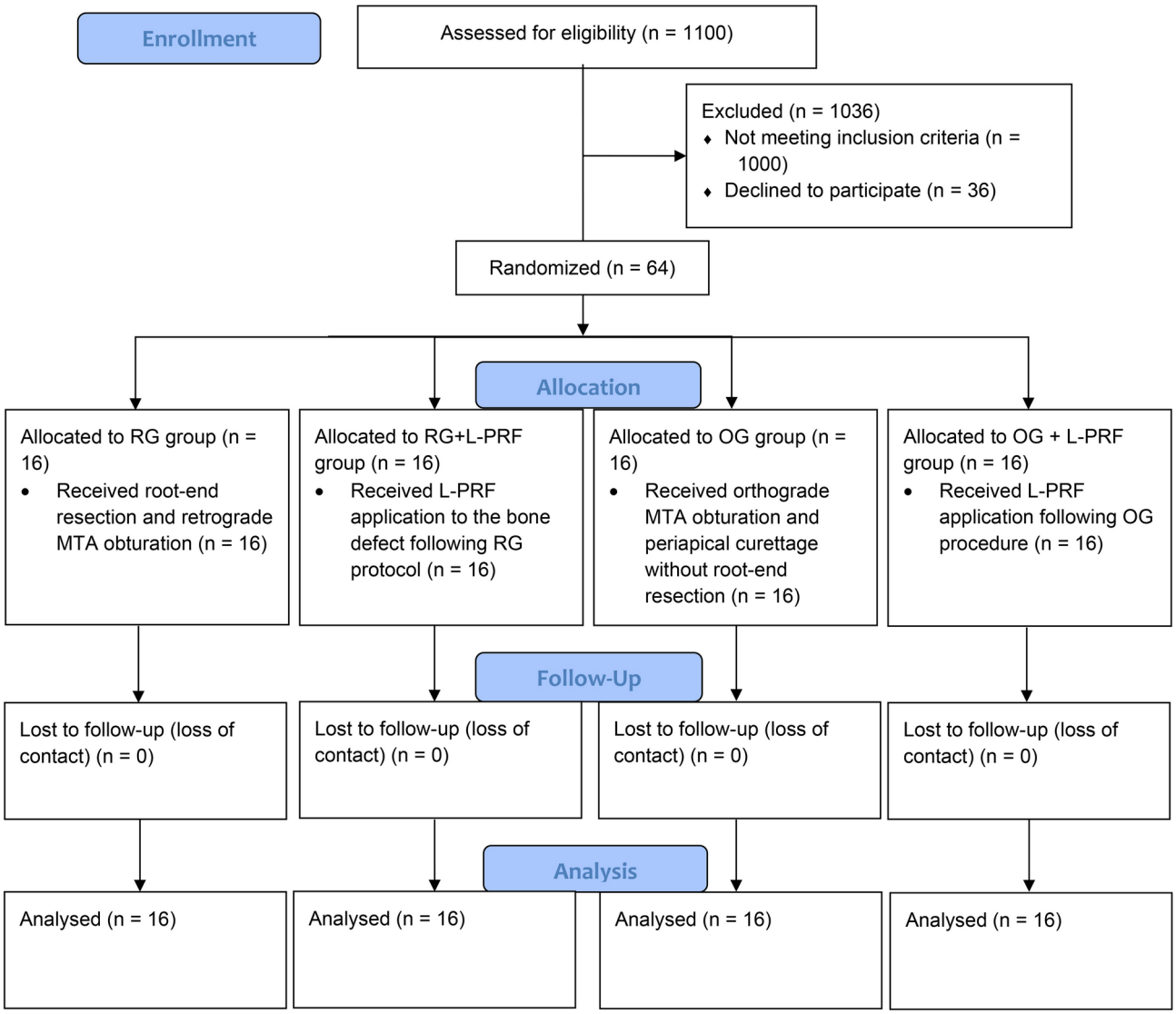


Fig. 1. CONSORT flow diagram.

- Allergy to penicillin.
- Use of steroids or nonsteroidal anti-inflammatory drugs within 48 h prior to treatment.

The scope of the study consisted of two parts: one focusing on clinical aspects and the other on radiological aspects. The diagnosis of apical periodontitis was based on patient history, clinical examination, and radiographic assessment. The clinical examination included a visual assessment of the tooth and surrounding tissues, periodontal probing, a palpation test, a percussion test, evaluation of existing restorations, and assessment of swelling, fistula, and tooth mobility. The demographic characteristics of the participants (age, gender, chronic disease status, medication use, smoking habit) and clinical findings (presence of swelling, tooth mobility, tenderness to percussion [T-PER], tenderness to palpation [T-PAL], and fistula, as well as pain score based on a visual analog scale [VAS]) were recorded preoperatively. The radiographic findings included tooth number, tooth type (incisor/canine/premolar), coronal restoration quality (adequate/marginal defect present), root canal obturation density (well condensed/poorly condensed), obturation level (under-obturation/over-obturation/adequate obturation), number of crowns, number of fillings, number of root canal obturations, and number of missing teeth. All parameters were recorded before and after surgery.

The presence of radiolucent images associated with the periapical region and radiographic bone loss was evaluated using panoramic (Vista Pano S-Durr Dental AG, Bissingen-Bietigheim, Germany) and periapical radiographs (using the parallel cone technique). Images were captured using a Kodak RVG 5200 digital radiography system and a CareStream CS2100 intraoral X-ray unit (Carestream Dental, Atlanta, GA) operating at 60 kVp and 7 mA with an exposure time of 0.25 s. The object-to-focus distance was maintained at 30 cm, and a film-holding instrument (Super-Bite Senso, Kerr Corporation, Orange, CA, USA) was used to ensure standardization. All periapical radiographs were imported into Adobe Photoshop 2023 software (Adobe Inc.,

San José, CA, USA) for analysis. To standardize measurements, images taken with a 25 mm × 35 mm RVG sensor were calibrated to a uniform size of 25 mm × 35 mm using the scale function in Photoshop. Lesion areas were then measured in square millimeters using the magnetic lasso tool based on pixel contrast, with manual adjustments to ensure accurate delineation. As an indicator of disease progression in all patient groups, the PAI scoring system was used for radiographic assessment of apical periodontitis[21]. The largest diameter of the lesion was recorded as periapical lesion size (PLS), and the PALA (mm^2) was also measured. Prior to the study, the examiners were calibrated on a set of sample radiographs representing varying degrees of periapical lesions to ensure the consistent application of the PAI scoring system. Two calibrated investigators (YEH and AT) who were partially blinded to the patient groups performed all radiographic assessments under standardized conditions. Disagreements were resolved by discussion until a consensus was reached. Interexaminer reliability was calculated using Cohen's kappa.

Randomization and blinding

Sixty-four eligible patients were randomly allocated to one of the following four treatment groups (n = 16 per group) using a block randomization method implemented with a random number generator (www.random.org):

- Retrograde MTA obturation group (RG): Periapical curettage and apical resection were performed, followed by retrograde MTA application.
- Retrograde MTA obturation with L-PRF application group (RG + L-PRF): Periapical curettage and apical resection were performed, followed by retrograde MTA application and L-PRF application to the bone defect.
- Orthograde MTA obturation group (OG): Orthograde MTA application followed by periapical curettage without root-end resection.
- Orthograde MTA obturation with L-PRF application group (OG + L-PRF): Orthograde MTA application followed by periapical curettage without root-end resection and L-PRF application to the bone defect.

Due to the nature of the interventions, blinding of both the operator and the patient was not possible. Postoperative radiographic assessments were conducted by examiners partially blinded to the L-PRF applications, while clinical evaluations were performed by an independent blinded examiner.

Clinical procedures

All root canal retreatments were performed by the same experienced endodontist (SE) using a magnifying loupe (3.5 ×) in two sessions. After administering local anesthesia (articaine 4% with 1:200,000 epinephrine; Ultracaine DS Forte, Aventis, Istanbul, Turkey), the tooth was isolated with a rubber dam. All coronal restorations and carious defects were then removed, and access preparation was completed when the root canal obturation was properly exposed. Old root fillings were removed using Gates–Glidden drills (Dentsply Maillefer, Ballaigues, Switzerland) and endodontic files. The working length was established as 1 mm short of the apical foramen with an apex locator (Raypex6; VDW GmbH, Munich, Germany), and periapical radiographs were then taken to ensure that all obturation material had been removed. Root canals were prepared using VDW Rotate rotary files (VDW, Münich, Germany), and the master apical file was determined to be at least three sizes larger than the initial apical file or at least ISO-size 45, according to the canal size and anatomy[23]. Root canals were irrigated with 5 mL 5.25% NaOCl between each instrument change. Thus, a minimum of 30 mL irrigation solution was used for each canal. After instrumentation had been completed, the root canal was medicated with Ca(OH)2 (Calxyl; OCO Products, Dirnstein, Germany) and sealed with a 1-mm cotton pellet and at least a 3-mm layer of temporary filling material (Cavit G; 3 M ESPE AG, Seefeld, Germany). After 7 days, the tooth was isolated, and the temporary restoration as well as the medication were removed. The final irrigation was then made with 17% EDTA and distilled water. Completion of the root canal treatment proceeded with root obturation using lateral condensation of gutta-percha and AH Plus sealer (Dentsply Maillefer, Ballaigues, Switzerland) in the RG and RG + L-PRF groups. The root canals were orthogradely filled with mineral trioxide aggregate (MTA Angelus Indústria de Produtos Odontológicos S/A, Londrina, PR, Brazil) in the OG and OG + L-PRF groups. MTA apical plugs were delivered to the apical third of the canal using the microapical placement method. MTA plug material was loaded into the carrier (MAP One system, Produits Dentaires S.A., Vevey, Switzerland), delivered into the apical third in small batches, and condensed vertically with a prefitted hand plugger until a 3 mm apical plug was created. The remaining root canal was then obturated with gutta-percha and AH Plus sealer. Access cavities were restored with composite resin (Z250, 3 M Corporation, Saint Paul, MN, USA), and a final radiograph was taken.

All surgical procedures were performed by the same experienced oral and maxillofacial surgeon (SG) on the same day as the completion of the root canal obturation. Following the administration of infiltration local anesthesia (ultracain forte, 4% articaine with 1:100,000 epinephrine), a mucoperiosteal flap was reflected to expose the surgical site. A surgical window was created in the buccal bone using a medium-sized round steel bur under continuous irrigation with sterile saline while taking care to avoid damage to adjacent tooth apices to expose the root apex and periradicular lesion. The cortical window was enlarged to the margins of the lesion to eliminate any thin cortical bone. Granulation tissue and any other pathological tissues surrounding the root apex were removed using a curette. Patients allocated to the retrograde MTA obturation groups (RG and RG + L-PRF) underwent root-end resection. The apical 3–4 mm of the root was resected perpendicular to the long axis of the tooth using a fissure bur. An ultrasonic tip was used to prepare the root-end cavity for retrograde obturation. MTA was then delivered into the root-end cavity using the micro apical placement method described above. Patients allocated to the orthograde MTA obturation groups (OG and OG + L-PRF) received only apical curettage. All surgical sites were irrigated with saline, gelfoams were placed to fill the bone cavities in the OG and RG groups, and the flaps were repositioned and sutured using 4–0 Vicryl (polyglactin 910) suture material.

In patients assigned to the L-PRF application groups (OG + L-PRF and RG + L-PRF), 10 ml venous blood was collected from the participants' antecubital veins using anticoagulant-free glass vacutainer tubes. Importantly, the blood was rapidly centrifuged within 1–2 min after collection, before it started to clot. The tubes were centrifuged immediately (PC-02 centrifuge, Process Ltd, Nice, France) at 3000 rpm (RCF: 400g, fixed-angle:33°) for 10 min[24]. A structured fibrin clot was then obtained in the middle of the tube between the red corpuscles at the bottom and the acellular plasma at the top. The L-PRF clot was removed from the tube and placed in a special box to create a membrane. The L-PRF membrane was then applied to the apical bone defect.

Postoperative care

All patients were prescribed an antibiotic (amoxicillin-clavulanic acid, 1000 mg twice daily for five days), an analgesic (naproxen sodium, 550 mg twice daily as a rescue medication, to be taken as needed for pain), and a mouthwash (0.2% chlorhexidine gluconate, three times daily for one week). The sutures were removed after 7 days.

Outcome measurements

The patients were called for clinical and radiographic evaluation at 1 week and at 1, 3, 6, 9, and 12 months. PAI scores, PLSs, and PALA values were measured on periapical radiographs taken during the control sessions. Pain score, swelling, mobility, T-PER, T-PAL, and presence of fistula were also recorded. Details on the number of painkillers taken by the patients were sought, and the patients were asked to mark the pain they felt each day for 1 week postoperatively on a VAS ranging from 0 (no pain) to 10 (the worst pain imaginable).

Statistical analysis

Statistical analysis of the data was performed using SPSS software version 27.0 (IBM, Chicago, IL, USA). Categorical data were analyzed using the chi-square test. Due to the sample size ($n < 30$), nonparametric statistical analyses were employed. The Friedman test (nonparametric repeated measures ANOVA) was used to compare the nonparametric data of more than two dependent groups. The Kruskal–Wallis test was used to compare the non-parametric data of more than two independent groups. While the Spearman correlation test was used for non-parametric data in determining the relationship between independent variables, the Pearson correlation test was used for parametric data. In addition, prior power analyses were performed to determine the minimum number of subjects for the study. The nonparametric data were displayed using box plots, while the categorical data were displayed using bar charts. The Cohen's d value was used for the effect size of the study. Statistical significance was set at a p-value of less than 0.05.

Results

The post hoc analysis of the PALA scores at 1 month postoperatively showed a large effect size (Cohen's $d = 1.05$) between the groups. According to Cohen's conventions, this size (≥ 0.8) is considered a large effect, indicating a substantial difference between the groups.

Demographic data and baseline tooth-related characteristics

Table 1 presents the demographic and baseline tooth-related characteristics of the study groups. No statistically significant differences were observed between the groups for gender, age, smoking habit, tooth type, coronal restoration quality, or root canal obturation density ($p = 0.969$, $p = 0.6773$, $p = 0.925$, $p = 0.927$, $p = 0.700$, and $p = 0.301$, respectively; Table 1). Therefore, any observed differences in clinical and radiographic healing outcomes between the groups were considered independent of these demographic and dental characteristics.

Under-obturation was the most common type of root canal obturation observed (81.25% in the RG group, 75% in the RG + L-PRF group, 68.75% in the OG group, and 81.25% in the OG + L-PRF group), followed by over-obturation (12.5% in the RG group, 6.25% in the RG + L-PRF group, 18.75% in the OG group, and 12.5% in the

	RG (A)	RG + L-PRF (B)	OG (C)	OG + L-PRF (D)	p
n	16	16	16	16	
Gender, F (%)	8(50%)	7(44%)	7(44%)	8(50%)	[c]0.969
Age, years	32 ± 13 29(19–58)	34 ± 15 31(18–58)	31 ± 12 26(18–55)	33 ± 11 31(12–55)	[a]0.6773
Tooth type, n (Inc/Can/Prem)	6/2/8	6/2/8	5/1/10	4/1/11	[c]0.927
Smoking habit, n	3	3	2	4	[c]0.925
CRQ, n (Adeq/MDP)	12/4	14/2	14/2	13/3	[c]0.700
RCFD, n (Adeq/Inadeq)	11/5	14/2	13/3	12/4	[c]0.301

Table 1. Comparison of demographic data and baseline tooth-related characteristics among the RG, RG + L-PRF, OG, and OG + L-PRF groups. [a]Kruskal-Wallis Test (Nonparametric ANOVA) with post-test (Dunn's Multiple Comparisons Test). [c]Chi-square test. *If the p value obtained with the ANOVA test is < 0.05, the p values between the groups are determined (A-B, A-C, A-D, B-C, B-D and C-D, respectively). Nonparametric data were given as mean ± SD and median (min–max). SD: Standard deviation, F: Female, Inc/Can/Prem: Incisor/canine/premolar, CRQ: Coronal restoration quality, Adeq/MDP: Adequate/Marginal Defect Presence, RCFD: Root canal filling density, Adeq/Inadeq: Adequate / Inadequate.

OG + L-PRF group). Adequate obturation was the least common, occurring in 6.25% of the RG group, 18.75% of the RG + L-PRF group, 12.5% of the OG group, and 6.25% of the OG + L-PRF group.

Clinical evaluations

Preoperatively, there were no significant differences between the groups in terms of PAI, VAS scores, or the presence of swelling, mobility, T-PER, T-PAL, or fistula ($p > 0.05$; Table 2). At 1 week postoperatively, no statistically significant differences were observed between the groups in terms of postoperative PAI score, VAS score, swelling (Fig. 2A), mobility (Fig. 2B), T-PAL (Fig. 2D), or fistula ($p > 0.05$). However, the RG + L-PRF group exhibited significantly lower T-PER compared to the RG group ($p < 0.05$; Table 2**,** Fig. 2C). Similarly, no statistically significant differences were observed between groups for PAI or VAS score, swelling, mobility, T-PER, T-PAL, or fistula presence at months 1, 3, 9, and 12 postoperatively ($p > 0.05$).

Comparing the groups in terms of analgesic use, it was found that the RG + L-PRF group had a relatively lower number of patients receiving analgesics on the day of the operation and 1 week afterward. However, these differences between the groups were not statistically significant ($p > 0.05$; Table 3).

Radiographic evaluations

The PAI scores were not significantly different among the groups preoperatively or at 1 week, 1 month, or 12 months postoperatively ($p > 0.05$; Table 4). While no significant differences in PALA were observed preoperatively, significant intergroup differences were observed at 1, 6, and 9 months postoperatively ($p = 0.0260$, $p = 0.0069$, and $p = 0.0371$, respectively). Specifically, the RG + L-PRF group had significantly lower PALA values than the OG group at 1, 6, and 9 months postoperatively ($p < 0.05$, $p < 0.01$, and $p < 0.05$, respectively, Table 5, Fig. 3). To improve clarity and facilitate the statistical interpretation of changes in the PALA values of the patients, the percentage change (PALA healing percentage) was calculated over a 12-month period (months 1, 3, 6, 9, and 12) relative to immediate postoperative baseline values. There were statistically significant differences in PALA healing percentages between the groups at 1, 6, and 9 months ($p = 0.0008$, $p = 0.0078$, and $p = 0.0279$, respectively). The RG + L-PRF group consistently showed the highest PALA healing rates across all follow-up periods, while the OG group showed the lowest healing rates. At 1 month postoperatively, the RG + L-PRF group had statistically significantly higher PALA healing rates compared to the RG, OG, and OG + L-PRF groups ($p < 0.05$, $p < 0.001$, and $p < 0.05$, respectively). At 1, 3, 6, and 9 months postoperatively, the RG + L-PRF group

	RG (A)	RG + L-PRF (B)	OG (C)	OG + L-PRF (D)	p
n	16	16	16	16	
Preop					
VAS pain score	1 ± 1 1(0–2)	1 ± 1 1(0–3)	1 ± 1 1(0–3)	1 ± 1 1(0–4)	[a]0.9992
Swelling, n	4	3	3	5	[c]0.811
Mobility, n	3	3	4	5	[c]0.811
T-PER, n	8	6	8	8	[c]0.861
T-PAL, n	8	6	7	9	[c]0.740
Fistula, n	6	4	5	4	[c]0.844
Postop. 1st week					
VAS pain score	3 ± 3 2(0–8)	2 ± 3 2(0–9)	3 ± 3 3(0–9)	3 ± 3 3(0–9)	[a]0.7004
Swelling, n	3	2	4	2	[c]0.751
Mobility, n	4	1	3	2	[c]0.499
T-PER, n	9	2	8	4	[c]0.031
T-PAL, n	8	3	5	3	[c]0.171
Fistula, n	0	0	1	0	[c]0.384
Postop. 1st-12th months					
VAS pain score	0	0	0	0	-
Swelling, n	0	0	0	0	-
Mobility, n	0	0	0	0	-
T-PER, n	0	0	0	0	-
T-PAL, n	0	0	0	0	-
Fistula, n	0	0	0	0	-

Table 2. Comparison of clinical parameters among the RG, RG + L-PRF, OG, and OG + L-PRF groups at baseline, postoperative week 1, and months 1 and 12. [a]Kruskal-Wallis Test (Nonparametric ANOVA) with post-test (Dunn's Multiple Comparisons Test). [c]Chi-square test. If the p value obtained with the ANOVA test is < 0.05, the p values between the groups are determined (A-B, A-C, A-D, B-C, B-D and C-D, respectively). Nonparametric data were given as mean ± SD and median (min–max). SD: Standard deviation, Preop: Preoperative, Postop: Postoperative, VAS: Visual Analogue Scale, T-PER: Tenderness on percussion, T-PAL: Tenderness on percussion.

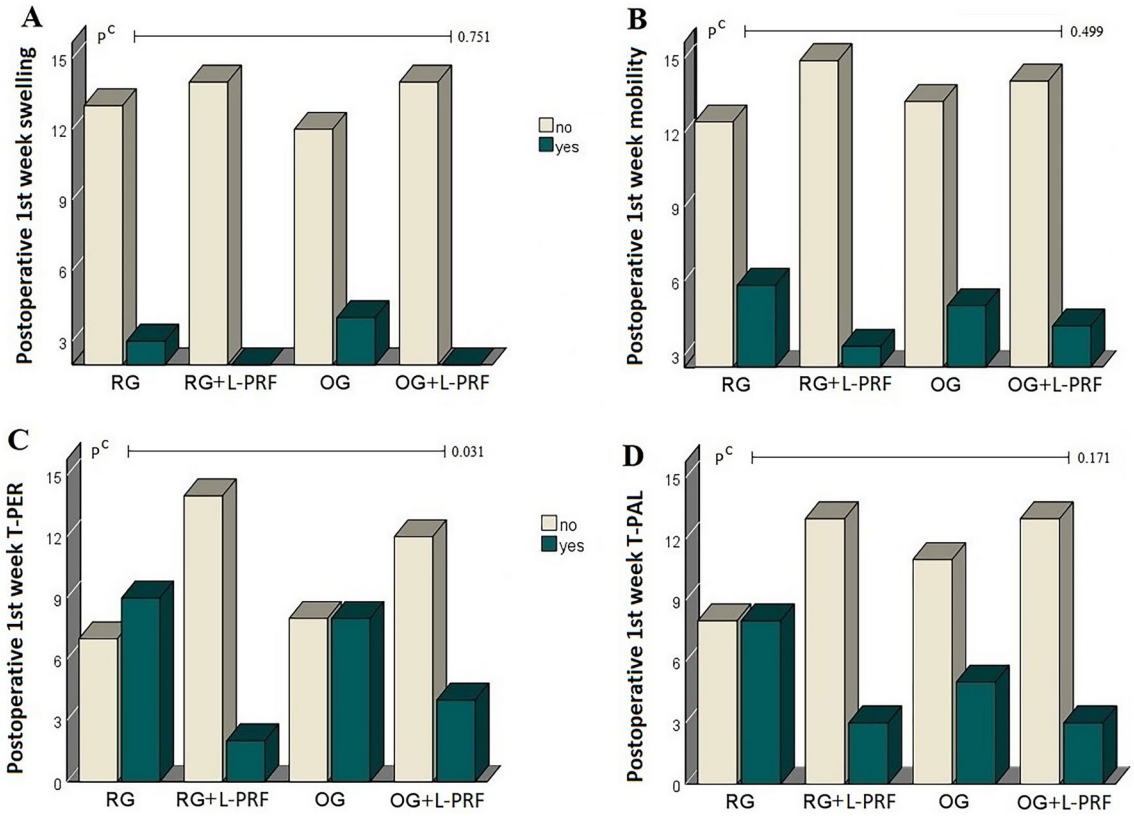


Fig. 2. Distribution of participants exhibiting swelling (**A**), tooth mobility (**B**), tenderness to percussion (**C**), and tenderness to palpation (**D**) at postoperative week 1 in the RG, RG + L-PRF, OG, and OG + L-PRF groups. c: chi-square test.

	RG (A)	RG + L-PRF (B)	OG (C)	OG + L-PRF (D)	p
n	16	16	16	16	
Op. day, n	1.4 ± 0.7 1.5(0.0–2.0)	1.2 ± 0.5 1.0(0.0–2.0)	1.2 ± 0.5 1.0(0.0–2.0)	1.25 ± 0.58 1.0(1.0–3.0)	[a]0.6377
Postop. 1st day, n	1.1 ± 0.9 1.0(0.0–2.0)	0.9 ± 0.6 1.0(0.0–2.0)	1.1 ± 0.9 1.0(0.0–3.0)	0,9 ± 0,9 1.0(0.0–2.0)	[a]0. 7868
Postop. 2nd day, n	1.0 ± 0.8 1.0(0.0–2.0)	0.8 ± 0.7 1.0(0.0–2.0)	0.9 ± 1.0 0.5(0.0–3.0)	0.8 ± 0.8 1.0(0.0–2.0)	[a]0.8934
Postop. 3rd day, n	0.4 ± 0.7 0.0(0.0–2.0)	0.2 ± 0.5 0.0(0.0–2.0)	0.6 ± 0.9 0.0(0.0–3.0)	0.5 ± 0.9 0.0(0.0–2.0)	[a]0. 4863
Postop. 4th day, n	0.4 ± 0.7 0.0(0.0–2.0)	0.2 ± 0.5 0.0(0.0–2.0)	0,5 ± 0,9 0,0(0,0–3,0)	0.3 ± 0.7 0.0(0.0–2.0)	[a]0.6328
Postop. 5th day, n	0.3 ± 0.7 0.0(0.0–2.0)	0.1 ± 0.5 0.0(0.0–2.0)	0,4 ± 0,9 0.0(0.0–3.0)	0.3 ± 0.7 0.0(0.0–2.0)	[a]0.3791
Postop. 6th day, n	0.1 ± 0.3 0.0(0.0–1.0)	0.1 ± 0.5 0.0(0.0–2.0)	0.3 ± 0.7 0.0(0.0–2.0)	0.2 ± 0.5 0.0(0.0–2.0)	[a]0.7514
Postop. 7th day, n	0.0 ± 0.0 0.0(0.0–0.0)	0.1 ± 0.3 0.0(0.0–1.0)	0.0 ± 0.0 0.0(0.0–0.0)	0.3 ± 0.6 0.0(0.0–2.0)	[a]0.0953

Table 3. Comparison of postoperative analgesic use among the RG, RG + L-PRF, OG, and OG + L-PRF groups in the first postoperative week. [a]Kruskal-Wallis Test with post-test (Dunn's Multiple Comparisons Test). [c]Chi-square test. *If the p value obtained with the ANOVA test is < 0.05, the p values between the groups are determined (A-B, A-C, A-D, B-C, B-D and C-D, respectively). Nonparametric data were given as mean ± SD and median (min–max). SD: Standard deviation, Op: Operation, Postop: Postoperative.

was followed by the OG + L-PRF and RG groups, which showed almost similar healing rates. The RG + L-PRF group also showed significantly higher PALA healing rates than the OG group at 6 and 9 months postoperatively ($p < 0.01$ and $p < 0.05$, respectively; Fig. 4). Both L-PRF application groups (RG + L-PRF and OG + L-PRF) had healing percentages greater than 90% at 9 months postoperatively. At 12 months postoperatively, all groups

	RG (A)	RG + L-PRF (B)	OG (C)	OG + L-PRF (D)	p
n	16	16	16	16	
Preop	5 ± 0 5(4–5)	5 ± 0 5(5–5)	5 ± 0 5(4–5)	5 ± 0 5(5–5)	[a]0.5657
Postop. 1st week	5 ± 0 5(4–5)	5 ± 0 5(5–5)	5 ± 0 5(4–5)	5 ± 0 5(5–5)	[a]0.5657
Postop. 1st month	5 ± 0 5(4–5)	5 ± 0 5(5–5)	5 ± 0 5(4–5)	5 ± 0 5(5–5)	[a]0.5657
Postop. 12th month	2 ± 1 1(1–3)	2 ± 1 1(1–3)	2 ± 1 2(1–3)	2 ± 1 2(1–4)	[a]0.3810

Table 4. Comparison of periapical index scores among the RG, RG + L-PRF, OG, and OG + L-PRF groups at baseline, postoperative week 1, month 1, and month 12. If the p value obtained with the ANOVA test is < 0.05, the p values between the groups are determined (A-B, A-C, A-D, B-C, B-D and C-D, respectively). Nonparametric data were given as mean ± SD and median (min–max). SD: Standard deviation, Postop: Postoperative. [a]Kruskal-Wallis Test (Nonparametric ANOVA) with post-test (Dunn's Multiple Comparisons Test). [c]Chi-square test.

	RG (A)	RG + L-PRF (B)	OG (C)	OG + L-PRF (D)	p
n	16	16	16	16	
Preop	29.7 ± 13.4 26,9(14,6–65,9)	33.5 ± 9.4 32.5(21.9–54.3)	31,5 ± 11,1 31.8(11.6–55.9)	32.9 ± 17.5 30.1(13.1–75.9)	[a]0.5978
Postop. 1st month	20.1 ± 6.8 18.7(10.5–38.8)	15.5 ± 4.8 15.2(7.3–25.3)	24.4 ± 9.1 26.5(7.6–39.9)	22.3 ± 10.3 19.0(6.2–41.3)	[a]0.0260
*Comparison p > 0.05, > 0.05, > 0.05, < **0.05**, > 0.05, > 0.05					
Postop. 3rd month	13.8 ± 5.9 13.2(5.8–26.3)	9.8 ± 6.5 10.8(0.0–21.0)	15.7 ± 7.7 17.5(3.4–29.8)	15.9 ± 8.5 17.2(3.4–29.8)	[a]0.2412
Postop. 6th month	7.5 ± 5.2 7.6(0.0–15.1)	4.1 ± 3.6 3.7(0.0–12.4)	10.9 ± 4.9 11.0(2.3–20.1)	7.0 ± 9.0 4.6(0.0–32.4)	[a]0.0069
*Comparison p > 0.05, > 0.05, > 0.05, < **0.01**, > 0.05, > 0.05					
Postop. 9th month	4.1 ± 3.9 3.8(0.0–10.1)	1.6 ± 1.5 1.7(0.0–4.1)	5.7 ± 4.6 4.5(0.0–16.2)	3.1 ± 4.6 0.0(0.0–13.9)	[a]0.0371
*Comparison p > 0.05, > 0.05, > 0.05, < **0.05**, > 0.05, > 0.05					
Postop. 12th month	1.4 ± 2.1 0.0(0.0–6.9)	0.3 ± 0.6 0.0(0.0–1.7)	2.7 ± 3.6 1.1(0.0–10.3)	1.7 ± 2.7 0.0(0.0–6.9)	[a]0.1475

Table 5. Comparison of periapical lesion areas (mm^2) among the RG, RG + L-PRF, OG, and OG + L-PRF groups at baseline and at each follow-up visit. [a]Kruskal-Wallis Test with post-test (Dunn's Multiple Comparisons Test). [c]Chi-square test. *If the p value obtained with the ANOVA test is < 0.05, the p values between the groups are determined (A-B, A-C, A-D, B-C, B-D and C-D, respectively). Nonparametric data were given as mean ± SD and median (min–max). SD: Standard deviation, Preop: Preoperative, Postop: Postoperative.

achieved over 90% PALA healing rates without any statistically significant differences; notably, the RG + L-PRF group exhibited almost complete healing, with a 99% healing rate (Figs. 4 and 5).

Correlational analyses

In the correlation matrix analysis based on the preoperative period, it was determined that there was a positive low-to-moderate correlation between preoperative T-PAL and preoperative swelling (rs = 0.3673, 95% CI: 0.1262–0.5674, p < 0.0001), preoperative mobility (rs = 0.3673, 95% CI: 0.1262–0.5674, p < 0.0001), and preoperative T-PER (rs = 0.5608, 95% CI: 0.3588–0.7126, p < 0.0001) values (Table 6). Similarly, there was a low positive correlation between preoperative T-PER and preoperative swelling (rs = 0.4412, 95% CI: 0.2120–0.6244, p = 0.0003). These findings were expected because the correlations between all these parameters were related to inflammation.

Discussion

The success of endodontic treatment relies on the complete healing of periapical tissues. Many periradicular lesions heal uneventfully after standard endodontic treatment[25]. In most cases in which the poor quality of root canal obturation leads to failure, nonsurgical endodontic retreatment tends to yield favorable results[1]. It has been reported that the complete and partial healing rates of periradicular lesions after nonsurgical endodontic therapy are 94.4%, with an overall success rate of up to 85%[26]. However, the presence of persistent symptoms, sinus tracts, and periapical lesions that cannot be treated with nonsurgical methods requires periradicular surgery to eliminate the source of infection[27].

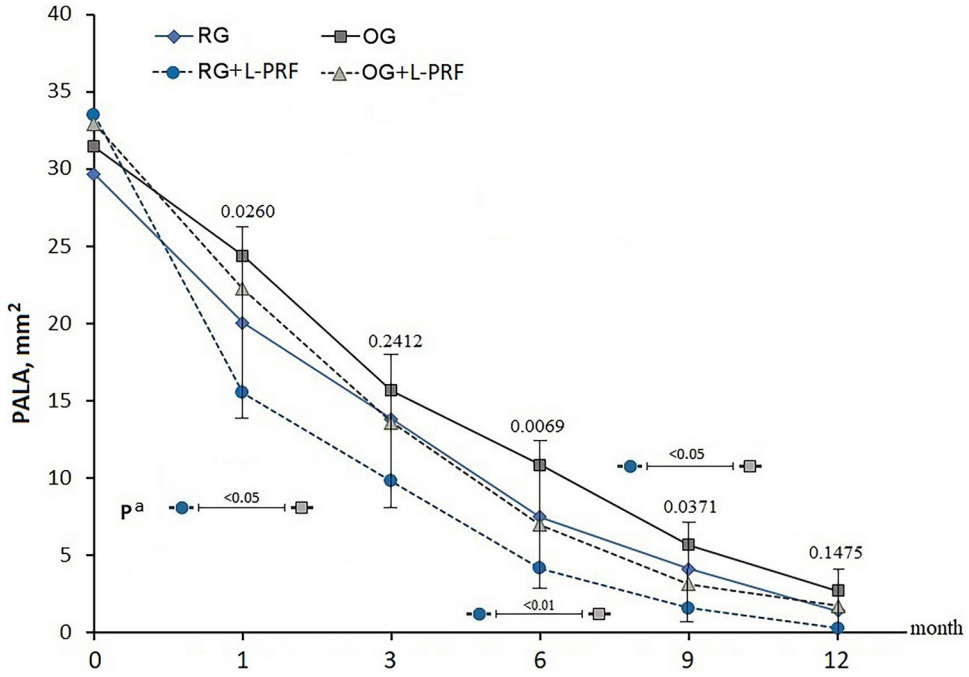
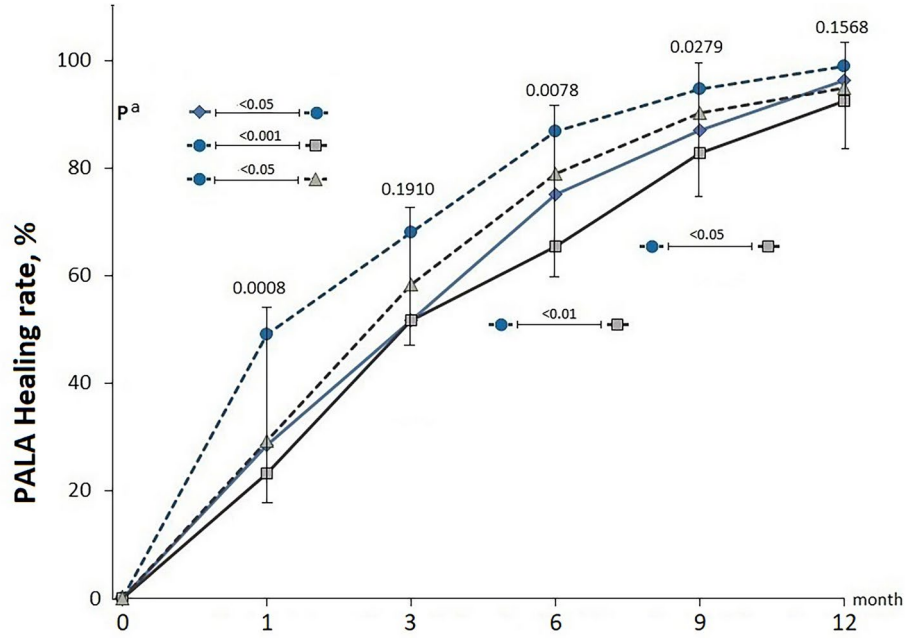


Fig. 3. Mean periapical lesion areas (mm^2) at follow-up appointments in the RG, RG + L-PRF, OG, and OG + L-PRF groups. a: Kruskal–Wallis test with post hoc test (Dunn's multiple comparison test).



RG	0,0	28,6	51,7	75,1	87,0	96,3
RG+L-PRF	0,0	50,7	68,0	86,9	94,6	98,9
OG	0,0	23,2	51,8	65,5	82,7	92,5
OG+L-PRF	0,0	29,3	58,3	79,0	90,3	94,9

Fig. 4. Mean periapical lesion healing rates (%) at follow-up appointments in the RG, RG + L-PRF, OG, and OG + L-PRF groups. a: Kruskal–Wallis test with post hoc test (Dunn's multiple comparison test).

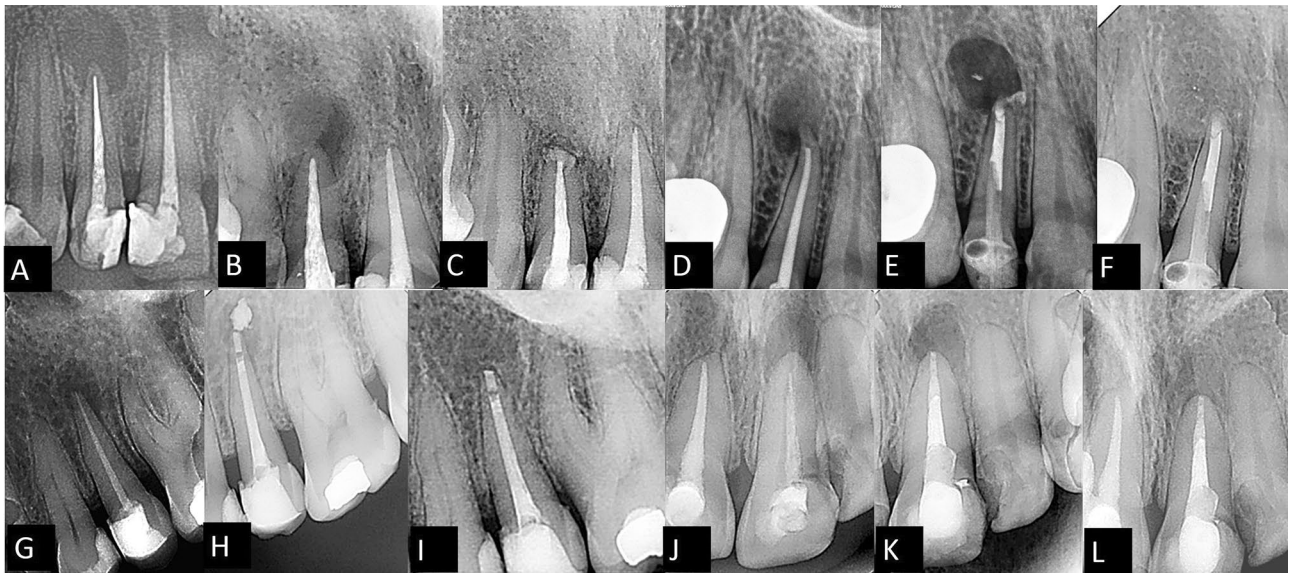


Fig. 5. Preoperative, immediately after retreatment, and 1-year postoperative radiographs of RG (**A**–**C**), RG + L-PRF (**D**–**F**), OG (**G**–**I**), and OG + L-PRF (**J**–**L**) groups.

n: 185	A:	B:	C:	D:	E:	F:	G:	H:
A:Preop PAI	1.000							
B:Preop VAS	0.134	1.000						
C:Preop Swelling	0.099	0.066	1.000					
D: Preop Mobility	0.099	− 0.011	0.129	1.000				
E:Preop T-PER	− 0.011	0.275	**0.441**	0.072	1.000			
F:Preop T-PAL	− 0.011	0.079	**0.367**	**0.367**	**0.561**	1.000		
G:Preop Fistula	− 0.080	0.030	0.044	0.125	0.143	0.212	1.000	
H:Preop PALA	0.203	− 0.149	0.230	0.039	− 0.005	0.167	0.051	1.000

Table 6. Correlation Matrix Results of Preoperative Findings. Significant values are in bold. Correlation matrix analysis: Depending on whether the data are parametric or not, the evaluation is repeated with Pearson (r) or Spearman (rs) correlation analyses. In this study, correlations found to be ≥ 0.30 were considered to be significant.

Periradicular surgery is influenced by several factors, including the complexity of the case, the type of surgical technique employed, and the use of adjunctive regenerative procedures. Although the most common method is an apicoectomy, apical curettage, which is characterized by the removal of inflammatory and pathological tissues without resecting the root tip, seems a more conservative treatment modality, particularly for teeth with compromised crown–root ratios[4]. However, comparative studies evaluating the efficacy of apical curettage remain limited.

The mechanism of bone healing after apical surgery is a complex and dynamic process consisting of a series of biological events. Modern surgical techniques, supported by biomaterials such as platelet-rich fibrin, can augment the healing process in periradicular surgery[7]. L-PRF, an autologous immune concentrate with a three-dimensional matrix structure rich in platelets, leukocytes, cytokines, and stem cells, gradually releases growth factors, thereby supporting soft and hard tissue healing by stimulating cell migration, adhesion, proliferation, and differentiation. Platelet-rich fibrin has also been reported to stimulate mitogenic responses in the periosteum and facilitate bone repair during the natural wound healing process[28]. L-PRF acts as a natural antimicrobial agent due to the activity of bioactive elements and leukocytes trapped in the fibrin matrix. Platelets release antimicrobial peptides and growth factors that inhibit the growth of various oral pathogens[13]. Furthermore, leukocytes can support the immune response and aid in the elimination of harmful microorganisms[29].

Considering the limited evidence of the effectiveness of periapical curettage, this study compared the efficacy of this technique with the apicoectomy technique in the treatment of apical periodontitis and evaluated the effect of L-PRF augmentation on the success of both surgical methods.

In almost all follow-ups, no statistically significant differences were observed between the groups for most clinical parameters. However, at the first postoperative week, the T-PER rates of the RG + L-PRF group were statistically significantly lower than those of the other groups. While other clinical parameters, including PAI and VAS scores, T-PAL, swelling, mobility, and fistula rates, were also lower in the RG + LPRF group,

these differences were not statistically significant. Additionally, the RG + L-PRF group was followed by the OG + L-PRF, OG, and RG groups in terms of T-PER, T-PAL, and mobility rates, respectively, in week 1. The clinical findings from the first postoperative week suggest that the RG + L-PRF method exhibits greater efficacy in short-term symptom reduction and clinical improvement. This finding highlights the ability of L-PRF to control inflammation, thereby increasing patient comfort during the early healing period. This significant early clinical improvement may be attributed to the synergistic effects of the biological benefits of L-PRF and the mechanical advantages of retrograde MTA obturation. The retrograde application route and the effective sealing created by the MTA biomaterial in the apical region, providing a barrier against the reentry of bacteria, are elements that support the healing of lesions. Additionally, L-PRF, a physiological fibrin matrix, acts as a scaffold for stem cells, especially during the phase of increased angiogenesis, and serves as an immune network that stimulates defense mechanisms. L-PRF possesses chemotactic properties for platelet and leukocyte cytokines, which are key to the immune system. These cytokines are stored within the fibrin structure to be slowly released into the environment[24,30,31]. Fewer symptoms were observed in the OG group compared to the RG group, to which L-PRF was not applied. This difference may be attributed to the increased surgical volume associated with root-end resection, which potentially leads to more severe inflammatory responses.

In this study, the differences between the groups regarding analgesic use during the postoperative first week were not statistically significant. However, the RG + L-PRF group tended to require fewer analgesic doses. The fibrin matrix of L-PRF contains various growth factors and cytokines that can promote tissue regeneration and modulate the inflammatory response, potentially contributing to reduced pain and improved healing outcomes[32–34]. The finding that L-PRF application provides an additional advantage in postoperative pain control aligns with previous studies[13,15,16,35]. However, some studies have reported only minimal or negligible pain reduction with L-PRF application in apical surgery[17,20]. This contradiction can be explained by multiple factors beyond the local biological effects of L-PRF, including individual pain thresholds, psychological factors, and the severity of surgical trauma.

A reduction in the size of the periapical lesion area is one of the most important outcomes for successful periapical healing. In this study, while there were no significant differences in preoperative PALA values between the groups, significantly lower PALA values were observed in the RG + L-PRF group compared to the OG group at 1, 6, and 9 months postoperatively. Therefore, the null hypothesis is partly rejected. The PALA healing rates obtained by comparing PALA values at follow-ups with immediate postoperative PALA values also support these results. The PALA healing rates of the RG + L-PRF group were statistically significantly higher than those of all other groups at 1 month postoperatively and higher than those of the OG group at months 6 and 9. At month 12, the differences in PALA healing rates between the groups were not significant. Across all follow-ups, the smallest PALA values and the highest PALA healing rates were observed in the RG + L-PRF group, while the largest PALA values and the lowest PALA healing rates were observed in the OG group. The RG + L-PRF group exhibited PALA healing rates of 86.9%, 94.6%, and 99% at 6, 9, and 12 months, respectively. Both L-PRF-applied groups (RG + L-PRF and OG + L-PRF) had PALA healing rates exceeding 90% at 9 months. These results suggest that L-PRF can be an effective biomaterial that accelerates bone healing in periapical surgical treatments, especially when combined with an apicoectomy.

Most studies conducted in various fields of oral and maxillofacial surgery, including implant treatment, periodontal regeneration, third molar surgery, guided bone regeneration, socket preservation, and maxillary sinus augmentation, have demonstrated the positive effects of adjuvant use of L-PRF on bone healing. L-PRF fibrin matrix is responsible for the slow release of growth factors (epidermal growth factor, transforming growth factor-β, platelet-derived growth factor, vascular endothelial growth factor, insulin growth factor-1, fibroblast growth factor) that regulate mesenchymal cell migration and proliferation as well as matrix proteins (thrombospondin-1, fibronectin, and vitronectin) over 7–14 days during the proliferative phase of wound healing. L-PRF is considered a promising biomaterial for promoting bone regeneration due to its ability to increase bone formation and improve bone architecture by stimulating osteoblast proliferation, differentiation, and migration through growth factors[36–38]. The results of the few clinical controlled studies evaluating the efficacy of L-PRF in endodontic surgery are controversial. This study's findings align with previous research reporting the positive effects of PRF on periapical surgery in terms of periapical bone density and hard tissue healing[13–16]. On the other hand, some researchers have reported that PRF had no significant effect on the radiologic healing of apical defects[18,19].

Apicoectomy is generally considered a necessity and an essential part of periapical surgical procedures. An endodontically treated tooth will exhibit a restoration success rate of 97.5% when the endo-post length is equal to or greater than the crown length[6]. However, in the absence of a proper relationship between crown and root, root-end resection can compromise the stability of the tooth in the socket and negatively affect the stability of the restoration. In such cases, an alternative treatment approach may involve performing apical curettage without an apicoectomy. Apical curettage can be considered an intermediate form of trepanation and apicoectomy. The complete removal of granulomatous tissue and foreign material from the periapical region provides the infection-free environment necessary for successful tissue regeneration. The advantage of the apical curettage procedure is that the total root length is preserved, while long-term tooth stability is not compromised[4]. To our knowledge, there are several case reports in the literature reporting favorable results of the apical curettage technique without root-end resection in endodontic surgery for chronic periodontitis[4–6,8]. Additionally, the apical curettage technique was applied in a study[39] evaluating the efficacy of hydroxyapatite and platelet-rich plasma application to the apical cavity and in a case series[7] in which PRF was applied to apical defects.

Salcedo et al.[6] and Fadhilah and Santosa[8] reported positive results of a 6-month clinical and radiographic follow-up of cases treated with root canal retreatment and apical curettage, emphasizing the possibility of tooth preservation with this technique in cases in which root-end resection would compromise the endo-post length and impair tooth stability in the alveolus. Srivastava[4] reported that apical curettage combined with root canal

treatment was a successful procedure in resolving a periapical lesion in a case with recurrent sinus formation and pus discharge. Altonen and Hakala[5] reported satisfactory 3-year follow-up results in 18 patients with acute periapical infection perforating the cortical bone. These patients underwent simultaneous root canal obturation and apical curettage, which emphasizes that radiological healing rates differ depending on the initial lesion size. In the present study, the PALA values of the OG + L-PRF group and the RG group were similar from the third month onwards, and the PALA healing rates were similar across all follow-ups. This finding suggests that apical curettage combined with L-PRF application to the bone cavity may serve as an effective treatment alternative in cases in which the crown-to-root ratio is impaired so as not to jeopardize the long-term stability of the tooth.

In a previous study evaluating periapical healing based on radiographic changes, lesion sizes were categorized as follows: small lesions measured 0–5 mm, medium lesions measured 6–10 mm, and large lesions were defined as greater than 10 mm in diameter. The study reported that an average time of 6.4 months was required for the healing of small lesions, 7.25 months for medium lesions, and 11 months for large lesions[40]. Based on this information and considering the effect of initial lesion diameter on radiographic healing, patients with medium or large periapical lesions were enrolled in this study and were followed for 12 months to evaluate the effects of different apical surgical techniques and L-PRF application to bone defects on clinical and radiographic healing.

Limitations of the study

The limitations of this study include the small sample size, the inability to blind patients, and the inability to blind the researcher during radiographic assessments. A lack of blinding introduces potential bias. Ethical considerations prevented the collection of blood samples from groups in which L-PRF was not applied, thus precluding patient blinding to the L-PRF application. Similarly, the nature of the surgical procedures precluded blinding the investigators performing the radiological assessments to the surgical techniques. While there were no statistical differences between the study groups regarding age, sex, and patient complaints, the data were based on patient statements. Prospective studies with larger sample sizes are needed to validate patient-reported outcomes. The radiological evaluations were performed using two-dimensional periapical radiographs to assess the improvement in periapical radiolucency, and histological analysis of the healing tissue could not be performed due to ethical concerns. Future studies that include evaluation with three-dimensional imaging techniques may provide a more comprehensive understanding of the healing process. This study did not consider the duration of surgery, which can affect postoperative pain and edema. Further studies should investigate the effect of the duration of root-end resection and apical curettage surgery on postoperative clinical parameters and patient comfort.

Conclusions

Combining root-end resection and retrograde MTA obturation with L-PRF application to apical bone defects represents an effective treatment strategy for periapical lesions, optimizing both short- and long-term healing. This approach appears particularly advantageous in cases involving large periapical lesions. However, in cases in which the crown-to-root ratio is unfavorable and may jeopardize long-term tooth stability, periapical curettage combined with orthograde MTA obturation and L-PRF application to the defect offers a viable, less invasive treatment alternative.

Data availability

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Received: 24 December 2024; Accepted: 3 March 2025
Published online: 08 March 2025

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Funding

This work was funded by Istanbul Medipol University, #2022-05.

Declarations

Competing interests

The authors declare no competing interests.

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