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Treatment outcome of perforation repair with bio-ceramic based materials: A retrospective study

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Treatment outcome of perforation repair with bio-ceramic based materials: A retrospective study

A thesis submitted in partial fulfillment of the requirements for the degree of Master of Science in Dentistry at Virginia Commonwealth University.

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Abstract

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INTRODUCTION: The aim of this retrospective cohort study was to assess the treatment outcome of orthograde perforation repair using bio-ceramic based materials.

METHODS: Data from the VCU graduate endodontic practice were analyzed retrospectively. Treatment had been conducted by VCU endodontic residents under the supervision of qualified endodontists during the period from August 2014-December 2020. All cases in which a bio-ceramic based material had been used as a perforation repair material were included. Bio-ceramic based materials included MTA, EndoSequence Root Repair Material Putty and Paste (ERRM), and iRoot BP Plus Root Repair Material (BP-RRM). Perforation repair was performed using a dental operating microscope. Two calibrated examiners assessed the radiographic outcome 6 to 24 months after treatment. The relationship between the pre-operative factors and treatment outcome was analyzed using binary logistic regression analysis.

RESULTS: Forty-seven cases were initially identified from August 2014 to December 2020. Of these, 24 cases were examined at follow-up (51% recall rate). Overall, 16 of the included teeth (66%) were classified as healed/healing, and 8 teeth (33%) were classified as non-healing. The

results of the binary logistic regression analysis showed that none of the 7-pre-operative variables included in the model were significantly associated with the outcome ($p > 0.05$).

CONCLUSION: Based on the binary logistic regression model, newer calcium silicate-based materials, ERRM and BP-RRM, are comparable to the clinical performance of MTA in perforation repair procedures**.**

Keywords: root perforation, MTA, ERRM, BP-RRM, treatment outcome, calcium silicate-based materials

Introduction

Root perforation is an iatrogenic or pathologic communication between the root canal system and the oral cavity or tooth supporting tissues (1). Root perforation can be caused by iatrogenic accidents during dental treatment or by pathologic processes including root resorption or dental caries (2). Iatrogenic root perforations may occur during endodontic or prosthodontic treatment (3). In fact, almost an equal split was found between the incidence of iatrogenic root perforations created during endodontic treatment (47%) and prosthodontic treatment (53%) (3).

Several factors have been reported to predispose to iatrogenic accidents during dental treatment (2). These include calcified canals, pulp stones, exaggerated or misdirected access cavity, extra-coronal restorations, the presence of intracanal posts, and tipping or rotation of teeth (2). Like any other endodontic mishap, a root perforation creates a significant therapeutic challenge facing the endodontist that may contribute to a poor prognosis. In fact, an earlier study investigating the reasons for extraction of endodontically treated teeth found that 4.2% of teeth were extracted due to iatrogenic root perforations (4).

Early diagnosis and immediate management of root perforations are crucial to prevent negative consequences of root perforations (5). These include inflammatory responses associated with the periodontal supporting structures and subsequent alveolar bone destruction (2, 5). Depending on the severity of the inflammatory reaction, it might result in granuloma formation, epithelial proliferation, and periodontal pocketing (2, 5).

The diagnosis of a root perforation is based on clinical and radiographic examinations (5). Clinically, the diagnosis of a root perforation is a challenging process (5). However, a few clinical signs may be indicative of a possible perforation. These include persistent bleeding

during the access opening, persistent bleeding during the root canal preparation after the removal of the pulp tissue, and blood impregnation of the paper point (5). Yet, certain systemic conditions, blood thinning medications, teeth with immature apices, and internal resorption may be associated with excessive bleeding, and therefore, the clinicians should keep this in mind when making the diagnosis of root perforation (2, 6). The apex locator is a useful technological resource that has an important role in diagnosing root perforations (7).

Radiographic examination has a vital role in the management of endodontic complications including root perforations (5). Peri-apical radiographs (either film-based or digital) are widely used in endodontic diagnosis, treatment, and follow-up. A radiolucency associated with a suspected perforation site is a frequent radiographic finding (5). However, the inherent limitations of this imaging modality that arise from two-dimensional (2D) projection of three-dimensional (3D) objects, can reduce the diagnostic efficacy of the conventional radiography due to geometric distortion, and the limited information on the extension, size, and location of a lesion.

The introduction of cone-beam computed tomography (CBCT) in endodontics is an evolutionary step that aids in the diagnosis and management of different pathologic and iatrogenic conditions during endodontic treatment. In an earlier study, Shemesh et al. evaluated the overall accuracy of CBCT scans versus peri-apical radiographs (PRs) in detecting strip and mechanical root perforations in the mesial roots of endodontically treated mandibular molars (8). The results showed that CBCT scans were significantly more accurate in detecting strip perforations when compared to PRs (8). On the other hand, no statistically significant difference was found between CBCT scans and PRs in detecting mechanical root perforations (8). In fact, CBCTs' detection of root perforations in endodontically treated teeth might pose a challenge.

CBCTs' diagnostic errors are usually detected in association with high density objects due to scattering and beam hardening effects. These metallic artifacts constitute potential risks for misdiagnosis, especially when a root perforation is suspected.

In another study, D'Addazio et al compared the accuracy of conventional PRs with CBCT in the detection of simulated endodontic complications in non-endodontically treated teeth (9). The examined endodontic complications were separated instruments, external resorption, and root perforations (9). The results showed that overall CBCT was significantly superior to conventional PRs in the detection of many endodontic complications (9). However, there was no significant difference between CBCT and conventional PRs in the detection of root perforations (9). In fact, based on Takeshita et al study, PRs was the recommended imaging modality to diagnose root perforations (10). Therefore, the clinicians should keep in mind that there is no ideal imaging modality for the detection of root perforations, and the diagnosis of root perforations should be made in conjunction with clinical findings.

Historically, the prognosis of a perforation repair has been poor (6). This was especially true before the introduction of the dental operating microscope and bio-ceramic based dental materials in the endodontic field (11, 12). Unfortunately, the visualization of the perforation site can be difficult even with the use of the microscope. Various dental materials have been used over the years for perforation repair (2). These included amalgam, gutta-percha, glass ionomer cement, zinc ethoxy-benzoic acid cement, and intermediate restorative material (2). However, many of these materials demonstrated poor biocompatibility and sealing ability (2). In fact, root perforation was the second most common cause of failure associated with endodontic therapy (6). In 1967, Seltzer and Bender reported that the frequency of root perforations ranged from 3% to 10%, however, the true frequency of root perforations at that time was probably higher

especially before the introduction of the microscope and electronic apex locators in endodontic practices (13).

Based on studies conducted before the 1990s, only 3 preoperative factors: time, size, and location of the perforation, were thought to be clinically relevant in the prognosis and healing of root perforations (14, 15, 16, 17, 18). The time between the perforation and the perforation repair was considered to be a significant factor in the healing process (14, 15). Better healing outcomes were achieved in cases with immediately sealed root perforations (14,15). This was probably true because in immediately well-sealed perforations, the chance of infection was dramatically decreased (5). Therefore, a better peri-radicular environment around the perforation site is established.

The size of the perforation was another important prognostic factor in the healing of root perforations (5). A smaller perforation size was associated with a better healing outcome (16, 17). Himel et al. conducted an animal study evaluating the treatment outcome of mandibular posterior teeth with perforations using 3 materials (16). The results showed that the tooth size in relation to the perforation size was directly proportional to the treatment outcome, and that larger teeth had the best outcomes (16). Small perforations are easier to seal effectively without extruding the sealing materials into the surrounding tissues (5, 16, 17).

The location of the perforation in relation to the crestal bone has been considered to be the most important factor affecting the outcome of perforation repair (5). Crestal bone perforations are thought to have a poor prognosis probably due to the contamination of the perforation site with the oral flora and subsequent epithelial migration and pocket formation (18). Therefore, root perforations located apical to the crestal bone should have a better prognosis since the perforation site is sealed and protected from the oral flora (5, 17, 18).

In newer studies assessing perforation repair outcomes, additional prognostic factors were tested including gender, number of roots, tooth type, tooth location, presence or absence of radiolucency adjacent to the perforation site, clinical signs and symptoms, periodontal defects, type of treatment, apical periodontitis, and cause of the perforation (2, 19, 20). However, based on the results of a recent systematic review and meta-analysis regarding the treatment outcome of root perforation repairs, only 2 factors were found to be statistically significant (2). These were tooth location (maxilla or mandible) and the presence or absence of a radiolucency adjacent to the perforation site (2).

One of the most important advances in the field of endodontics was the introduction of bio-ceramic based materials in the 1990s. A bio-ceramic material can be defined as a ceramic product used in the dental and medical fields that have osteo-inductive properties (21). Mineral trioxide aggregate (MTA) was the first dental bio-ceramic material introduced in the market. To overcome the drawbacks of MTA including long setting time and handling properties, several bio-ceramic materials were developed based on tricalcium silicate chemistry. These have included EndoSequence Root Repair Material Putty and Paste (ERRM), and iRoot BP Plus Root Repair Material (BP-RRM).

A number of clinical studies have been conducted to assess the perforation repair potential of MTA (2). Based on the results of these studies, MTA seems to be the material of choice for sealing root perforations (2). The overall success rate of perforation repair using MTA was around 80% (2). On the other hand, the overall success rate of perforation repair regardless of the materials used was around 70% (2). Based on the results of numerous outcome studies of perforation repair, MTA, which is a bio-ceramic based material results in better healing outcomes when compared to other materials including gutta percha, conventional glass ionomer,

resin-modified glass ionomer, IRM, amalgam, and retroplast (2, 19, 20). Unfortunately, the literature lacks clinical studies assessing the perforation repair potential of newer bio-ceramic based materials including EndoSequence Root Repair Material Putty and Paste (ERRM), and iRoot BP Plus Root Repair Material (BP-RRM).

The aim of this retrospective cohort study was to assess the treatment outcome of orthograde perforation repair using bio-ceramic based materials.

Materials and methods

The study protocol was approved by the Institutional Review Board (IRB) at Virginia Commonwealth University (VCU) (study # HM20019170). Data from the VCU graduate endodontic practice were analyzed retrospectively. Treatment had been conducted by VCU endodontic residents under the supervision of qualified endodontists during the period from August 2014-December 2020. All cases in which a bio-ceramic based material had been used as a perforation repair material were included. Bio-ceramic based materials included MTA, EndoSequence Root Repair Material Putty and Paste (ERRM), and iRoot BP Plus Root Repair Material (BP-RRM).

Inclusion and Exclusion Criteria

The inclusion criteria were: (1) patients who had orthograde root perforation repair using a bio-ceramic based material and (2) a minimum of a 6-month follow-up since the perforation repair appointment. Patients with compromised immune status including diabetic and pregnant participants, those who refused to participate, or those with incomplete records were excluded. Teeth diagnosed with a longitudinal root fracture, a crack extending to the pulpal floor, or showed evidence of a periodontal-endodontic lesion on the day of perforation repair appointment were also excluded.

Perforation Repair Technique

The treatment was provided by VCU endodontic residents under rubber dam isolation. A dental operating microscope was used throughout the treatment session including the perforation repair procedure. The detection of a perforation was aided by an electronic apex locator (EAL) or by taking a periapical (PA) radiograph with a K file. Before sealing the perforation site, it was

irrigated with 5.25% sodium hypochlorite and then with sterile saline. Afterward, the perforation site was dried with sterile paper points or cotton pellets. All the included cases were completed in 2 visits with calcium hydroxide used as interappointment medicament, and the access cavities were temporarily sealed using either Cavit or IRM. The perforation repair procedure was performed during the first or second visit.

The MTA cement, ERRM, or BP-RRM was applied to the perforation site using an amalgam carrier (in case of MTA use) or a glick instrument (in case of ERRM and BP-RRM use). The material was compacted in the perforation defect using the plugger on one end of glick instrument. In case of a furcation perforation repair, a layer of vitrebond was placed over the repaired site. None of the included cases used an absorbable matrix during the repair procedure. All the cases were obturated using gutta percha and a root canal sealer via continuous wave technique. Root canal sealers used in the present study included Tubli-Seal, Sealapex, Kerr, and EndoSequence BC Sealer. After completion of the root canal treatment, the access cavities were sealed using either Cavit, IRM, or composite resins.

Pre-operative Data

The patients' baseline characteristics and preoperative date were gathered from the patient's records and radiographs. The baseline characteristics of the patients included: age, and gender (male or female). Based on the results of an earlier systematic review and meta-analysis regarding the treatment outcome of root perforation repair, 5 preoperative factors were selected. The selected preoperative factors were tooth location (maxilla or mandible), radiolucency adjacent to perforation site (present or absent), nature of treatment (primary treatment or retreatment), timing of the perforation repair (immediate, < 1 month, > 1 month, or unknown), and location of the perforation to the level of crestal bone (crestal, supra-crestal, or sub-crestal).

Based on the meta-analysis results, tooth location and radiolucency adjacent to perforation site factors were found to significantly affect the success rate of orthograde perforation repairs (2).

In the same meta-analysis study mentioned above, the other 3 factors, including nature of treatment, timing of the perforation repair, and location of the perforation relative to the level of crestal bone, were found to be non-significant factors (2). However, due to the limited number of studies included in the meta-analysis when assessing the earlier 3 factors, the statistical power to identify any truly significant factors might have been compromised (2). Therefore, these factors were reassessed in the present study. Two additional preoperative factors were included in this study which were the pre-operative measurements of the periodontal probing depths and the repair material used. This factor was included to assess the effect of the pre-operative periodontal condition of the perforated tooth on the outcome of perforation repair procedures.

Treatment Outcome

Treatment outcomes were based on clinical and radiographic findings. The periapical index (PAI) proposed by Orstavik was used to assess the peri-apical area (22). To assess the area adjacent to a perforation site, a simple scoring system was used (perforation index (PI)). The scoring system consisted of 3 categories based on the size of the widest diameter of a radiolucency adjacent to a potential perforation site (in mm). The 3 categories were: A (0-2 mm), B (>2-4 mm), and C (>4 mm). The evaluators were instructed to assign each radiograph to a category. For each subject post-operative images, taken after the completion of the root canal treatment, and follow-up digital periapical images were evaluated by 2 independent clinically experienced endodontists (GM, VM). The evaluation was done independently in a random sequence to assess the area adjacent to the perforation site and any pathological changes in the periapical areas.

The treatment outcome was dichotomized into healed/healing and non-healing. A case was classified as healed/healing when the following criteria were met: no clinical signs or symptoms and no radiolucency or reduction in the size of a radiolucency peri apically or at the perforation site at the follow-up appointment. On the other hand, a case was classified as non-healing if the clinical examination revealed the presence of signs or symptoms and/ or the radiographic examination showed no change or an increase in the size of a radiolucency peri-apically or at the perforation site at the follow-up appointment. The clinical statuses of the included teeth were evaluated by the endodontic residents at the follow-up appointments.

Calibration

Both endodontists were calibrated for the PAI and PI use. Any disagreement between the two evaluators was resolved by re-assessing the radiographic findings, re-appraisal, and discussion until a mutual consent was reached.

Inter- and intra-rater reliability (PAI and PI)

To examine the inter- and intra-rater reliability, the 2 evaluators were asked to complete the radiographic assessment of the 24 subjects twice within a 2-week interval.

Sample Size Calculation

Sample size calculation was performed using G*Power version 3.1.9.7 software. The effect size was calculated based on the study results of Main et al. (19), who found that the clinical success rate of perforation repair using MTA was 100%. Since the literature lacks clinical studies assessing the perforation repair potential of EndoSequence Root Repair Material Putty and Paste (ERRM), and iRoot BP Plus Root Repair Material (BP-RRM), the success rate was assumed to be 70%. The latter percentage, i.e., 70%, was selected based on the systematic

review results of Siew et al. (2), who reported that the overall success rate of perforation repair regardless of the materials used was around 70%. Based on 80% power (β level = 0.20) and a significance level of $\alpha = 0.05$, the minimum sample size was calculated to be 22 teeth per group for a total of 44 teeth. To compensate for possible dropouts, an additional 10% was added to the calculated sample size. Therefore, a total sample size of 48 (24 per group) was included.

Statistical Analysis

Statistical analyses were conducted using Statistical Package for Social Science software (Version 25; SPSS Inc., Chicago, IL, USA). The level of significance was set at $p < 0.05$. Kappa coefficient was calculated to assess the Inter- and intra-rater reliability. The proposed criteria by Landis and Koch for interpretation of kappa coefficient was used: ≥0.75, excellent; 0.4–0.75, fair to good; and <0.4, moderate or poor (23). The relationship between the pre-operative factors and treatment outcome was analyzed using binary logistic regression analysis. The results of the logistic analysis were described using adjusted odds ratios (OR) and 95% confidence intervals (CI).

Results

Forty-seven cases were initially identified from August 2014 to December 2020. Of these, 24 cases were examined at follow-up (51% recall rate). The sample size was composed of 14 (58.3%) women and 10 (41.7%) men. The mean (standard deviation) age of the patients was 53.8 (19.5) (Shapiro-Wilk test > 0.05). Overall, 16 of the included teeth (66%) were classified as healed/healing, and 8 teeth (33%) were classified as non-healing.

Kappa coefficient demonstrated fair to good inter rater agreement ($PAI1_{GM,VM} = 0.46$, ($p < 0.05$), $PAI2_{GM,VM} = 0.50$ ($p < 0.05$), $PI1_{GM,VM} = 0.52$ ($p < 0.05$), and $PI2_{GM,VM} = 0.57$ ($p < 0.05$)).

Since none of the included perforations were supra-crestal in location, the pre-operative variable, location of the perforation relative to the level of crestal bone, was recategorized into crestal or sub-crestal perforations before conducting the binary logistic regression analysis. Also, the pre-operative variable, timing of the perforation repair, was recategorized into immediate, < 1 month, or > 1 month since the timing of the perforation repair was known for all the included cases. Table 1 showed the results of the binary logistic regression analysis. None of the 7-pre-operative variables included in the model were significantly associated with the outcome ($p > 0.05$).

Table 1. Association between treatment outcome and pre-operative factors: binary logistic regression				
Independent variable	**(n)**	**OR**	**95% CI**	***P* value**
Repaired material				
MTA	11	0.38	0.32-4.63	>0.05
ERRM or BP-RRM	13	ref.	ref.	
Tooth location				
Maxilla	16	0.43	0.02-7.78	>0.05
Mandible	8	ref.	ref.	
Radiolucency adjacent to the perforation site				
Presence	13	0.43	0.04-4.19	>0.05
Absence	11	ref.	ref.	
Nature of treatment				
Primary treatment	16	0.19	0.01-3.34	>0.05
Retreatment	8	ref.	ref.	
Duration of perforation repair				
Immediate	14	9.22	0.29-288.87	>0.05
<1 month	4	1.63	0.037-71.6	
>1 month	6	ref.	ref.	
Location of perforation to level of crestal bone				
Crestal	9	0.97	0.1-9.59	>0.05
Sub-crestal	15	ref.	ref.	
Pre-operative periodontal probing depths				
Within 3 mm	17	0.08	0.005-1.55	>0.05
More than 3 mm	7	ref.	ref.	
OR, adjusted odd ratio; CI, confidence interval Hosmer-Lemeshow goodness-of-fit, $p > 0.05$				

Discussion

In this retrospective clinical study, the treatment outcome of orthograde perforation repair using bio-ceramic based materials was investigated. To the best of our knowledge, no prior studies have evaluated the repair potential of newer bio-ceramic based materials, including ERRM and BP-RRM.

The study recall rate of 51% was lower than recall rates achieved by earlier studies (20, 24, 25). Earlier studies suggested that the high number of relocated subjects in large cities can be responsible for lower recall rates (25, 26). Moreover, many patients were hesitant to show up for their recall appointments in this period due to COVID-19 pandemic.

The follow-up period used in the present study can be considered sufficient to detect any radiographic changes in the periodontal condition surrounding the root apices or adjacent to the perforation sites. However, this period is insufficient to detect complete healing of bone lesions especially on PA radiographs. Therefore, this issue was addressed when assessing the radiographs by including the healing category to the treatment outcome. Nevertheless, a lower healing rate was expected in the present study (66%) in comparison to the earlier outcome studies since subtle bony changes might not be detected on the PA radiographs as in CBCT (24, 25, 27). Despite the fact that there is no ideal imaging modality for the detection of root perforation, recent studies demonstrated the superior performance of CBCT in detecting subtle bony changes over a short period of time (27).

PAI is a validated and reproducible index for the assessment of the periapical tissues (22). However, PAI is not suitable to assess the area adjacent to the perforation sites, therefore, a simple perforation index was used based on the size of the widest diameter of a radiolucency

adjacent to a potential perforation site (in mm). Both evaluators (GM, VM) were calibrated on the use of both PAI and PI before the radiographic assessment was carried out.

Based on the binary logistic regression model, none of the included pre-operative factors had a significant effect on the healing rate. This might be due to the limited number of cases included in the present study, and the short follow-up period. However, the present study aimed at including new patients and further follow-up examinations in the future. Therefore, the pre-operative factors will be reevaluated.

Regarding the location of perforation site in relation to the crestal bone, none of the included cases were supra-crestal perforations. This was expected since supra-crestal perforations are best repaired with materials that are resistant to oral fluids like Geristore since the calcium silicate-based materials will be washed out if it is in contact with oral fluids (2). Also, the timing of the perforation repair was known for all the included cases, and this was predictable. The data of the present study was obtained from a residency practice in a school setting, and all the patients were referred from either the dental school students or outside referrals.

All the 8 cases that were classified as diseased showed radiographic evidence of periodontal breakdown around either the root apices or the perforation sites. Nevertheless, only 2 cases were symptomatic, and clinically were tender to percussion and biting. None of the 8 non-healing cases were extracted. Therefore, the present study demonstrated a 100% survival rate of teeth receiving orthograde perforation repair procedures.

Conclusions

Although the present study was limited by the small sample size, the results showed that (1) there was a high survival rate of orthograde perforation repair procedures using calcium silicate-based materials; (2) based on the binary logistic regression model, newer calcium silicate-based materials, ERRM and BP-RRM, are comparable to the clinical performance of MTA in perforation repair procedures; and (3) an acceptable success rate for the treatment of perforation repair can achieved with calcium silicate-based materials. In conclusion, further clinical studies with longer follow-up period are needed to further assess the newer calcium silicate-based materials.

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