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Article

Critical Factors Affecting Outcomes of Endodontic Microsurgery: A Retrospective Japanese Study

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Abstract: The critical preoperative and intraoperative factors that affect the success of endodontic microsurgery (EMS) in Japanese patients are not defined. We conducted a retrospective study that analyzed treatment outcomes for 46 teeth in 46 Japanese patients. Treatment was provided between March 2013–March 2015; all patients were evaluated after one year. Healing was assessed on the basis of clinical symptoms and radiographs. With the use of a binary logistic regression model to quantify success, we estimated the effects of patient age, sex, dental arch, lesion size, lesion type, previous root canal treatment, presence or absence of a post core, and presence or absence of an isthmus on the surgically prepared dentine surface. The overall success for EMS was 93.5% after one year; failures comprised 6.5%. Successful outcomes were higher ($p=0.04$) for maxillary teeth than for mandibular teeth. Success was higher ($p=0.019$) for patients who received root canal instrumentation prior to EMS. Age, sex, lesion size, lesion type, the presence or absence of a post core, and the presence or absence of a root canal isthmus had no effect ($p>0.2$) on success. We conclude that the percentage of successful outcomes after EMS treatment for Japanese patients presenting with periapical periodontitis is very high after one year and that success is influenced strongly by the dental arch and previous root canal instrumentation.

Keywords: endodontic microsurgery; root canal treatment; isthmus preparation; Short-term outcomes

1. Introduction

Non-surgical endodontic therapy is currently the most favored treatment method for clinical management of periapical periodontitis [1]. Despite positive outcomes associated with non-surgical treatments, a certain proportion of interventions fail [2–6] for an array of reasons including the presence of residual bacteria in difficult-to-instrument root canal systems and the presence of extra-apical infection [7]. In these cases, surgical endodontic treatment is often employed. One of the indicated surgical approaches is endodontic microsurgery (EMS) performed with a microscope, which provides higher proportions of successful outcomes than traditional root-end surgery [8]. This improved success may arise from the rigorous application of defined surgical procedures, more advanced instrumentation, improved retrograde root canal cavity preparation and filling materials, and high-resolution identification of underlying structural problems enabled by microscopy [9–11].

The percentage of successful outcomes following EMS is affected by several pre-treatment factors, which include root canal instrumentation prior to apicoectomy [12]. While previous instrumentation has been associated with improved outcomes, placement of a post and core

restoration has been reported to negatively affect prognosis [13]. Currently, no definitive conclusions have been reached with respect to these factors. In addition, if an isthmus is present on the surgically prepared surface of the root, isthmus preparation may be performed, but the effect of this preparation on post-treatment success is not defined [14,15]. While the therapeutic value of EMS is recognized in Japan [15,16], no studies have quantified outcomes and the relative importance of the pre-treatment factors described above. Here we conducted a retrospective analysis with one year follow-up of the preoperative and intraoperative factors that affect the success of EMS in Japanese patients.

2. Materials and Methods

2.1. Study Design

This study was conducted according to the principles of the Declaration of Helsinki (2013). Written, informed consent was obtained from all patients, and the study was approved by the Tokyo Dental College Institutional Review Board (Tokyo Dental College Ethical Review No. 515). Retrospective analysis of outcomes was conducted for patients who underwent microscope-guided apicoectomy in the Department of Conservative Dentistry of the Tokyo Dental College at Chiba Hospital between March 2013 and March 2015.

2.2. Sample Selection

Based on the medical and dental histories, patients who fulfilled the following inclusion criteria were selected.

1. No medical contraindications for surgical endodontic therapy (ASA-PS class I or II).
2. Diagnosis of periapical periodontitis by preoperative cone-beam computed tomography (CBCT).
3. Root resection and retrograde root canal filling were conducted with the aid of a surgical microscope and with specialized instruments and treatment protocols optimized for EMS.
4. The patient provided informed consent for the treatment.

Patients that exhibited root perforation, advanced marginal periodontitis, or root fracture during preoperative examinations were excluded from the study.

2.3. Surgical Treatment Procedures and Follow-up

All procedures were conducted by a single, board-certified endodontist with 15 years' experience. The same operative procedures were used for all patients enrolled in this study. Other than the performance of the incisions, procedures were conducted with a magnified view provided by a surgical microscope (OPMI PROergo, Carl Zeiss, Gottingen, Germany). Below we describe the surgical method.

Infiltration (for maxillary teeth) or block anesthesia (for mandibular teeth) was performed with 2% xylocaine with 1:80,000 epinephrine. Cognizant of the condition of the periodontal tissues and cosmetic appearance, releasing incisions were placed through the gingival sulcus and the gingival papilla. In some instances, an Ochsenbein flap design was used. A full thickness mucoperiosteal flap was reflected; low tractional forces were applied during the surgical procedure to aid visual inspection of the tooth root. If needed for improving visual access to the root apex, the labial surface of the alveolar bone was removed by osteotomy to expose the apex of the root and the lesion. A tapered fissure bur in a 45° angled-head air turbine drill was used to resect the root perpendicularly to its long axis at ~3 mm from the apex. After the apical portion had been severed from the root, the lesion was excised and immersed in 10% formalin solution. Hemostasis was conducted by applying pressure with a cotton swab soaked in 1:000 epinephrine. The cut surface was stained with methylene blue and examined under magnification. A 3 mm-deep retrograde cavity was prepared with an ultrasound tip (KIS Ultrasonic Tip, Obtura-Spartan, Fenton, MI). After enlargement, the cut surface was again stained with methylene blue and examined. Upon confirming there were no structural defects in the root, retrograde filling was conducted by inserting MTA cement (ProRoot MTA White,

Dentsply Tulsa Dental, Tulsa, OK). After placement of the filling, the integrity of the MTA seal was confirmed under magnification, and by obtaining radiographs of the affected site.

The flap was replaced and closed with interrupted sutures (6-0 nylon). After application of pressure and ice packs for 10 minutes, hemostasis was confirmed. All patients received amoxicillin hydrate (250 mg every 8 h for 3 days, starting immediately after the procedure) and either an anti-inflammatory analgesic (Loxoprofen sodium hydrate 60 mg) or Acetaminophen, 500 mg) every 6 h after surgery. The excised lesion was submitted for histopathological examination by a board-certified pathologist. The wound was disinfected with chlorhexidine and the sutures were removed on day 4. Patients who underwent surgery were contacted 12 months later and re-examined for assessment of healing. Patients who could not be contacted and those who declined to undergo re-examination were considered as lost to follow-up. At the 12 months examination, the presence or absence of signs and symptoms was evaluated, and dental radiographs were obtained.

2.4. Data Collection and Outcome Assessment

The following data were obtained from the patients’ records using the parameters identified below and recorded:

Age at surgery, sex, dental arch (maxillary or mandibular), lesion size, lesion type, preoperative root canal treatment, presence or absence of a post core, and presence or absence of an isthmus on the cut surface were recorded in the database. Preoperative and postoperative signs and symptoms (pain, and pain on percussion and palpation) and X-ray findings were also recorded in the database.

Patient assessments were conducted using postoperative dental radiographs and the criteria of healing of periapical lesions provided earlier by Rud *et al.* [17] and Molven *et al.* [18]. Based on these criteria, the status of periapical healing was classified as: complete healing, incomplete healing, uncertain healing, or unsatisfactory healing. Of these categories, complete healing and incomplete healing were assessed as “clinical success,” (Figure 1) and uncertain healing and unsatisfactory healing were considered as “clinical failure” (Figure 2). If the tooth had more than one root, the root that exhibited the least advanced healing was assessed as the overall status of healing for that tooth. Radiographs were evaluated by three calibrated, board-certified endodontists. If their assessments varied, they discussed the case until they reached a consensus assessment. The success rate was then calculated from this assessment.

If the tooth had more than one root, the root that exhibited the least advanced healing was assessed as the overall status of healing for that tooth. Radiographs were evaluated by three calibrated, board-certified endodontists. If their assessments varied, they discussed the case until they reached a consensus assessment. The success rate was then calculated from this assessment.

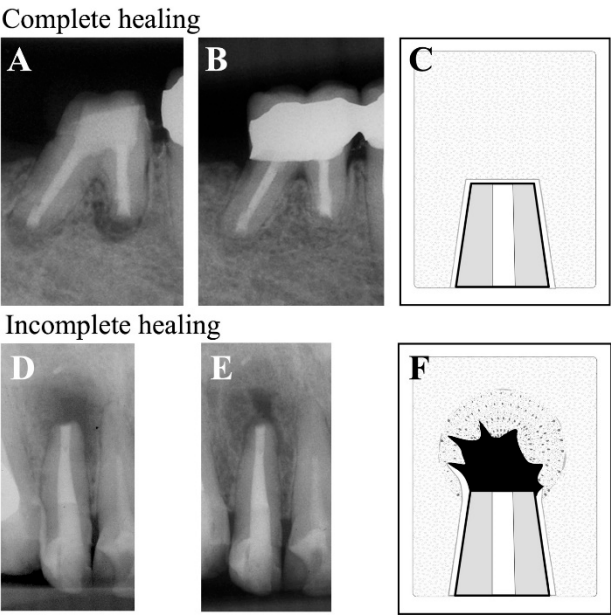


Figure 1. Representative radiographs as examples of clinical success. **Complete healing** (Top Row): A mandibular first molar was radiographically assessed as ‘complete healing’ 1 year after EMS. (A) immediate post-operative, (B) 1-year follow-up, (C) Diagram of the apical healing used for classification developed by Rud and Molven [17,18]. **Incomplete healing** (Bottom Row): A maxillary lateral incisor was radiographically assessed as ‘incomplete healing’ 1 year after EMS. (D) immediate postoperative, (E) 1-year follow-up, (F) Diagram of apical healing used for classification as described [17,18].

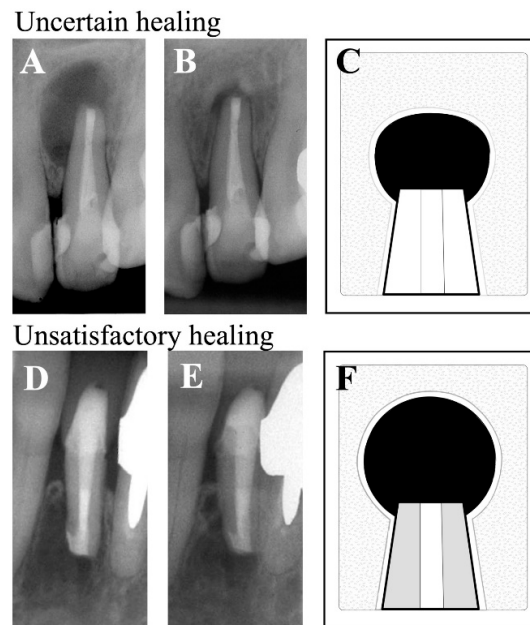


Figure 2. Representative radiographs as examples of unsatisfactory healing. **Uncertain Healing** (Top Row). A maxillary central incisor was radiographically assessed as ‘uncertain healing’ 1 year after EMS. (A) Immediate post-operative, (B) 1-year follow-up, (C) Diagram of apical healing used for classification as described [17,18]. **Unsatisfactory Healing** (Bottom Row). A mandibular lateral incisor was radiographically assessed as ‘unsatisfactory healing’ 1 year after EMS. (D) Immediate postoperative, (E) 1-year follow-up, (F) Diagram of apical healing used for classification as described [17,18].

2.5. Statistical Analysis

A binary logistic regression model was used in which the clinical healing rate was the dependent variable, which was used to evaluate associations between independent variables and treatment outcomes (“clinical success” versus “clinical failure”). The unadjusted odds ratios were calculated to evaluate the associations between variables. The effects of different variables on healing and their associations were evaluated using odds ratios and 95% confidence intervals.

EZR (Jichi Medical University Saitama Medical Center, Japan) was used for all statistical analysis [19]. EZR is a graphical user interface (GUI) for R (The R Foundation for Statistical Computing, Vienna, Austria); more precisely, it is the improved version of R Commander, which was designed to add statistical functions that are frequently used in biological statistics. For parametric data, the results are reported as mean±standard deviation.

3. Result

A total of 55 patients underwent EMS between March 2013 and March 2015, of whom 9 were excluded from the study. In two cases this was because root fracture was diagnosed intraoperatively, and the tooth was extracted; the other seven patients could not be contacted. The re-examination rate was 86.8% (46/53), and the final analysis set included 46 teeth of 46 patients. There were more than 2.5-fold more women ($n = 34$) than men ($n = 12$). The mean age of the patients was 46.2 ± 12.5 years.

According to the criteria described above for periapical healing after endodontic treatment [17,18], there was complete healing in 76.1% of cases (35/46), incomplete healing in 17.4% (8/46), uncertain healing in 2.2% (1/46), and unsatisfactory healing in 4.3% (2/46). Based on our working description of treatment success described above, clinically successful outcomes were 93.5% of cases and clinical failures comprised 6.5% of cases.

The mean lesion diameter was 5.2 ± 3.2 mm. Histopathological analysis showed that the excised lesions were of different pathological diagnoses (Table 1).

Table 1. Types of lesions removed during EMS.

Pathological diagnosis	n (%)
Radicular cyst	26 (65)
Radicular granuloma	8 (20)
Inflammatory granulation tissue	6 (7.5)
Not collected	6 (7.5)

We evaluated the association between healing outcome and prognostic factors (Table 2). There were more successful outcomes for teeth in the maxillary arch than for the mandibular arch (p=0.041). Treatment success was higher (p=0.019) when previous root canal instrumentation had been conducted than when no previous instrumentation was provided. There were no significant differences (p>0.2) of treatment success with respect to age, sex, lesion size on previous radiograph, the presence or absence of a post, or the presence or absence of a root canal isthmus.

Table 2. Distribution of Cases by Factor and Bivariate Analysis.

Variable/Factor (n)		Clinical success (%)	Clinical failure (%)	OR (95%CI)	P value
Sex (46)	Female	31 (67.4)	3 (6.5)	0	0.557
	Male	12 (26.1)	0 (0)	(0-7.012)	
Age, y (46)	< 45	29 (63.1)	2 (4.3)	1.035	1
	≥ 45	14 (30.4)	1 (2.2)	(0.02-.21.50)	
Arch (46)	Maxillary	39 (84.8)	1 (2.2)	17.08	0.041*
	Mandibular	4 (8.7)	2 (4.3)	(0.75-1165.82)	
Lesion size, mm (46)	< 5	17 (37)	0 (0)	Inf	0.524
	≥ 5	27 (58.7)	2 (4.3)	(0.11-Inf)	
Lesion type (34)	Granuloma	24 (70.6)	2 (5.9)	3.27	0.432
	Cyst	7 (20.6)	1 (2.9)	(0.04 -279.35)	
Pre-RCT (46)	Yes	33 (71.8)	0 (0)	Inf	0.019*
	No	10 (21.7)	3 (6.5)	(1.14-Inf)	
Post core (46)	Yes	17 (37)	2 (4.3)	0.561	0.561
	No	26 (56.5)	1 (2.2)	(0.01- 6.91)	
Isthmus (46)	Yes	18 (39.1)	2 (4.3)	0.368	0.572
	No	25 (54.4)	1 (2.2)	(0.01- 7.58)	

*Indicates significance (P<0.05); CI, 95% confidence interval.

4. Discussion

We examined Japanese patients who had undergone EMS one year previously for treatment of periapical periodontitis. We assessed the effects of preoperative and intraoperative factors on the percentage of successful outcomes after EMS, which was 93.5%, a result that is similar to previous reports [20–22]. As these earlier reports described analyses conducted on non-Japanese populations, the data collectively indicate that there are no substantial racial differences in EMS outcomes, at least with respect to Japanese populations. Further, of the pre-operative and peri-operative factors that were analyzed, only dental arch (maxillary or mandibular) and previous root canal instrumentation showed statistically significant differences with respect to the % of treatment success. The other

factors that were analyzed (lesion size, lesion type, presence or absence of a post core, presence or absence of an isthmus on the cut surface) did not affect treatment success.

We found no association between age or sex on the percentage of successful outcomes after EMS. A previous report indicated that successful outcomes were highest for younger patients in their 20s [23], and that the percentage of failed outcomes increased with age [13] while another report showed higher percentages of success for older patients [24]. Notably, other studies found no association with age [25,26]. With respect to the association with sex, one previous study reported that success was higher for women [27], whereas another found that successful outcomes were higher for men [13]. A study that used an insurance database to investigate treatment outcomes after apicoectomy found that the percentage of surviving teeth was higher for men than for women, and that the percentage of surviving teeth decreased continuously with the age of the patient [28]. In contrast, other studies found no significant differences with respect to age and sex [29–31]. Collectively, as the published literature on age and sex effects are inconsistent, these factors do not seem to influence the success of EMS.

In the current study the percentage of successful outcomes was higher for the maxillary arch than the mandibular arch, a result that may have been influenced by the relatively smaller sample size of teeth analyzed for the mandibular arch. Previous data indicated that the percentage of successful outcomes was higher for the maxillary arch than for the mandibular arch [13,32], and that success for the maxillary anterior teeth was reportedly higher than for posterior teeth in the maxilla. This difference may reflect the comparatively easier access and the less complex anatomical structure for anterior teeth [33].

In the current study, similar to previous analyses [34–36], the effect of lesion size was investigated by dividing lesions into two groups: radiographically detectable lesions with diameter <5 mm or lesions $\geq$ 5 mm. We found that mean lesion size was 5.20 mm and was not associated with any particular healing outcome one year later. Previous reports indicated the percentage of successful outcomes was positively associated with lesions of diameter <5 mm while lesions with a diameter $\geq$ 5 mm were not associated with success [37]. In contrast, longer term studies showed that lesion size did not affect the percentage of successful outcomes [17,38], which may reflect the notion that the time required for healing depends on lesion size [20]. Conceivably, healing by scarring (which we classified as “uncertain”) may exhibit periapical radiolucencies that shrink in diameter over longer time periods.

We found no effect on lesion type on the percentage of successful outcomes. Conceivably, this result may be influenced by our use of high magnification imaging during lesion removal, which is in contrast to previous studies in which this part of the procedure was conducted under none or low magnification. Previous data showed that radicular granulomas (73%) were more common than radicular cysts (15%) [39], which is similarly to the current study in which radicular granulomas (65%) were more common than radicular cysts (20%). In contrast, the opposite result was reported in another study in which chronic, non-specific inflammatory lesions and radicular cysts (47.3%) were more common than radicular granuloma (44.0%) [40]. Further, in this same study, treatment success for apicoectomy of teeth with cysts was higher than teeth with granulomas [40]. Conceivably, this outcome may reflect the notion that cysts, with epithelial cell walls, are relatively easier to remove than granulomas [41].

Previous root canal instrumentation can affect healing [7]. Similarly, we found that the percentage of successful outcomes was higher when root canal treatment was performed before EMS, a result that may reflect the reduced numbers of bacteria in the root canal system prior to initiation of EMS. In addition, previous treatment of the root canal aids can aid clinical diagnosis, thereby enabling the exclusion of teeth with root fracture or perforation, which facilitates positive treatment outcomes.

For many of the cases examined here, we found that EMS was indicated in cases exhibiting very little remaining tooth substance and in which post-core removal was challenging. But for these cases, there was no significant difference in the short-term percentage of successful outcomes, a result that is consistent with other studies [8]. In this context, when treatment was repeated for teeth requiring

post-core removal, vertical root fracture occurred more frequently than when EMS was performed [42]. This result could arise because post-core removal reduced the amount of dentin in the root, further weakening its resistance to fracture. Conversely, when EMS was performed on teeth with ideally restored post-cores, the long-term survival rate was higher [43]. Accordingly, while not yet resolved, previous root canal treatment is considered higher risk, and surgical treatment should be the first choice for teeth with an existing post-core.

The amount of dentin at the apex may affect treatment outcomes. Insufficient isthmus instrumentation may be one reason for the failure of apicoectomy [44]. If an isthmus is seen, certain authors encourage prophylactic enlargement and filling [44,45]. However, one study found that the four-year survival rate of teeth in which no isthmus was present and isthmus preparation was not conducted was 87.4%. This survival rate is higher than the 61.5% when an isthmus was present and isthmus preparation was conducted [14]. In addition, eight of the nine cases of failure in this study were associated with vertical root fracture after teeth had undergone isthmus preparation. These data suggest that isthmus preparation may reduce the amount of dentin remaining postoperatively and weaken fracture resistance. Notably, a micro-CT morphological study of the maxillary first molars of Japanese individuals found that, even when no isthmus was present or only an incomplete isthmus was observed at a position 3 mm from the mesiobuccal root canal apex, microscopic morphological structures associated with the outcome of root canal treatment, including isthmuses, were present more coronally [46]. For this reason, in the current study, if an isthmus was observed during apicoectomy ($n = 26/46$), whatever its shape, prophylactic isthmus preparation was conducted with a 0.5-mm-diameter ultrasound tip while being careful to remove the minimum amount of dentin. The one-year percentage of successful outcomes was not affected by isthmus preparation even though the tooth substance of the root is weakened after isthmus preparation and the possibility of root fracture may be increased [38].

EMS reportedly has a higher short-term success rate than non-surgical endodontic therapy [47], which is consistent with the data reported here. However, as with traditional root end surgery, the long-term success rate of EMS is lower (albeit only slightly) than other short-term estimates of treatment success [48,49]. Factors that are not manifest during the short-term can still affect the long-term prognosis. Therefore, additional, longer-term follow-up is needed.

5. Conclusions

The % of short-term successful outcomes after EMS in Japanese patients was very high (93.5%). The two factors that affected success were dental arch and previous root canal instrumentation. Age, sex, lesion size, lesion type, the presence or absence of a post core, and the presence or absence of a root canal isthmus had no significant effect on short-term success.

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Conflicts of Interest: The authors declare no conflict of interest.

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