Prognostic factors for clinical outcomes in endodontic microsurgery: three cohort studies and a randomized controlled study

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Prognostic factors for clinical outcomes in endodontic microsurgery: three cohort studies and a randomized controlled study

Directed by Professor Euiseong Kim

A Dissertation
Submitted to the Department of Dentistry
and the Graduate School of Yonsei University
in partial fulfillment of the
requirements for the degree of
Doctor of Philosophy of Dental Science

Minju Song

February 2013

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Feb 2013

Acknowledgements

Looking back my doctoral program for the last 3 years, I felt it was closer to the process of improvement of my mind not the process of learning. On reflection with finishing my program and writing acknowledgement, it seems to me that I always receive something not giving them. I realized that I have to express my thanks to many people. I apologize to them for just writing acknowledgement here instead of visiting and giving thanks to everyone.

For guiding my research and helping in the completion of my dissertation, I would like to express the deepest gratitude to my advisor, Prof. Euiseong Kim, He has encouraged, supported and advised me during my entire program. He is the model of a true teacher and has inspired me to be a better person and a better professional.

To Prof. Seung-Jong Lee I owe special thanks for his review and supporting my work. I also wish to thank Prof. Baek-Il Kim for his support and help and I am grateful to Prof. Hyeon-Cheol Kim for his kind review in spite of his busy schedule. I would like to express my most profound gratitude to Prof. Su-Jung Shin for all her indispensable advice and guidance.

I also want to thank Prof. Chan-Young Lee, Prof. Byoung-Duck Roh, Prof. Sung-Ho Park, Prof. Il-Young Jung for their help and support. My special appreciation goes to Prof. Jeong-Won Park for his help and advice. I also want to thank Dr. Yoo-Seok Shin, Dr. Ji-Hyun Jang for their help. I also thank Dr. Mina Park, Dr. Taekjin Nam, Dr. Su-Yeon Kim and Dr. Min-Ji Kang for their help.

I also owe special thanks to Prof. Chung-Mo Nam in the graduate school of public health of Yonsei University for allowing me attend his class.

Without everyone on the Department of Conservative Dentistry I would not have been able to enjoy and finish my program and I wish to thank everyone for their whole hearted support. To all my classmates, who gave me great support, I have appreciation and affection.

Finally, I wish to dedicate this work to Min-Young, Jae-Won and my parents. I am really grateful to my family for their support and love throughout my entire life. Whenever I was unsure and lost my confidence they believed in me and supported me through it.

December, 2012

By Author

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Abstract

Prognostic factors for clinical outcomes in endodontic microsurgery: three cohort studies and a randomized controlled study

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This dissertation aimed to examine the potential prognostic factors generally and investigate the effect of specific factors, root−end filling materials, and deficiency of periapical and marginal bone tissue, on the outcome of endodontic microsurgery.

1. Prognostic factors in endodontic microsurgery: a retrospective and a prospective cohort studies

The first purpose of this study was to examine the potential prognostic factors on the outcome of endodontic microsurgery and compared the predictors of an isolated endodontic lesion with those of both an isolated endodontic lesion and endodontic−periodontal lesion retrospectively and prospectively.

For a retrospective study, the data were collected from patients with a history of endodontic microsurgery performed between August 2004 and December 2008 and at least 1 year before being evaluated. Of the 907 cases, 491 were retained at follow−up. For a prospective study, data were collected between March 2001 and March 2011, a total number of 584 teeth requiring endodontic surgery were included in the study. Of the 584 cases treated, 431 cases came for recall after a period of at least 12 months. After surgery, an operation record form was made with the preoperative, intraoperative, and postoperative factors from the clinical and radiographic measures. For statistical analysis of the predisposing factors, the dependent variable was the dichotomous outcome (ie, success vs failure).

As a results, sex (female), tooth position (anterior), arch type (maxilla), lesion type (isolated endodontic lesion), and root−end filling material (mineral trioxide aggregate (MTA) and Super ethoxy−benzoic acid (Super EBA) were found to have a positive effect on the outcome. An isolated endodontic lesion might reduce the effect of many variables in the outcome of endodontic microsurgery, the tooth position (anterior), arch type (maxilla) and type of restoration (single/splinted crown, short bridge and RPD abutment) were found to be a pure positive predictor of an endodontic lesion affecting the clinical outcome.

2. MTA and Super EBA as root−end filling materials: a prospective randomized controlled study

The second purpose was to evaluate the clinical outcomes of endodontic microsurgery when Super EBA and MTA were used as the root−end filling materials in a prospective randomized controlled study.

Of the 388 teeth eligible for endodontic microsurgery between February 2003 and October 2010, 128 teeth were excluded from the study, and 260 teeth were randomly assigned to either the Super EBA group or the MTA group with equal numbers using the “minimization method.” Endodontic microsurgical procedures were performed according to the Yonsei protocol reported in a previous study and were carried out by a single operator. The patients were followed up at 3, 6, and 12 months. The primary outcome measure was the change in the apical bone density at 12 months, and the secondary outcome measures were the presence of clinical symptoms or abnormal findings at 12 months.

A total of 192 teeth were examined at the 12-month follow-up; 102 teeth were in the Super EBA group, and 90 were in the MTA group. The overall success rate was 94.3%, with a success rate of 95.6% (86/90 teeth) for MTA and 93.1% (95/102 teeth) for Super EBA. The statistical analysis of the success rate results did not show any significant difference between the groups (P =0.472)

3. Influence of deficiency of periapical and marginal bone tissue on clinical outcome: a prospective cohort study

The last purpose was to assess the influence of deficiency of periapical and marginal bone tissue on clinical outcome after endodontic microsurgery.

A total number of 199 teeth requiring endodontic surgery were included in the study between August 2004 and March 2011. During the surgical procedure, deficiencies of periapical and marginal bone tissue were measured just before the flap repositioned. With regard to the evaluated parameters, t-test and Mann-Whitney U test were performed to find differences between the 2 groups (success versus failure) for all parameters. In addition to these analyses, logistic regression model was performed with significant parameters which are assumed to be relevant clinically and statistically. And all measurements categorized, significant associations between the outcome and all the evaluation parameters were examined by a Pearson chi-square test or Fisher’s exact test with a significance level of 0.05.

A recall rate of 67.8% (135 of 199 teeth) was obtained and overall success rate was 85.2% (115 of 135 teeth). Absence or presence of buccal bone plate is potential predictors of the healing outcome, teeth with complete loss of buccal bone plate showed lower healing rate than those which are not (70.4% vs 88.9%, P = 0.029). And teeth with the buccal bone plate with > 3 mm showed a higher success rate than teeth with ≤ 3 mm (94.3% vs 66.7%, P = 0.002).

Factors influencing the outcomes of endodontic microsurgery may be diverse, but standardization of procedures can minimized its range. Patient and tooth-related factors such as sex, periodontal status and toot position are found to be prognostic, root-end filling material and type of postoperative restoration were also considered. More randomized controlled studies or prospective cohort studies concerning are needed to confirm these findings.

Key words : Endodontic microsurgery, apicoectomy, clinical study, randomized controlled study, prognostic factors, clinical outcome, mineral trioxide aggregate(MTA), super ethoxy-benzoic acid(Super EBA), bone defect, marginal bone loss, buccal bone plate

Prognostic factors for clinical outcomes in endodontic microsurgery: three cohort studies and a randomized controlled study

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I. Introduction

Endodontic treatment is a procedure for preventing or curing apical periodontitis caused by an infection of the root canal systems of affected teeth (Friedman, 1998). However, epidemiologic studies have reported that 33 to 60% of root-filled teeth in the population present with apical periodontitis (Eriksen et al., 2002). Nonsurgical retreatment is considered as the first treatment option in the management of persistent apical periodontitis (Siqueira, 2001). Endodontic surgery is indicated when nonsurgical retreatment is impractical or unlikely to improve on a previous result (Gutmann and Harrison, 1985). In particular, only surgical intervention might resolve the problem when a persistent lesion is related to a periapical cyst, a complex canal anatomy, extraradicular infections, or inadequate healing after nonsurgical retreatment (Karabucak and Setzer, 2007).

With the traditional technique that is the procedure before the accommodation of an operating microscope in endodontic field, the success rate of endodontic surgery is ranged from 43% to 75% (Mikkonen et al., 1983; Schwartz-Arad et al., 2003; Setzer et al., 2010), which is lower and not superior to those of nonsurgical retreatment (Torabinejad et al., 2009). In recent years, modern technique that include the use of magnification tools, ultrasonic instruments, and more biocompatible filling materials have been introduced (Creasy et al., 2009; Kim and Kratchman, 2006). These technical advances have increased the success rate compared with traditional root-end surgery; this success rate has varies considerably from 74% to 92% (Lindeboom et al., 2005; von Arx et al., 2003; Wang et al., 2004; Zuolo et al., 2000).

Endodontic microsurgery represents an evolutionary advance in periradicular surgery, applying not only modern ultrasonic preparation and filling materials but also incorporating microsurgical instruments, high-power magnification, and illumination (Kim and Kratchman, 2006). In addition, Setzer et al. (Setzer et al., 2012) specified endodontic microsurgery as endodontic surgery using ultrasonic root-end preparation, biocompatible root-end filling materials (Intermediate Restorative Material (IRM), Super ethoxy-benzoic acid (Super EBA), mineral trioxide aggregate (MTA)) and high-power illumination and magnification (10x and higher). Among the many studies on the clinical outcomes of surgical endodontics, there are only few reports related to endodontic microsurgery (Table 1). Moreover there are even fewer reports related to the prognostic factors of endodontic microsurgery.

Numerous authors have analyzed the effect of individual variables on the outcome of endodontic surgery. Most predictable prognostic factors in many studies include the age of the patient, existing root-filling length and quality and preoperative lesion size in preoperative factors; placement of root-end filling, root-end preparation method, root-end filling materials and operator

Table 1. Studies of endodontic microsurgery

Study	Sample size	Follow up period	Recall rate	Magnification	Root-end preparation	Root-end filling material	Success rate (%)	Methodology
Rubinstein & Kim(1999)	128	14 m	94/128	Microscope	Ultrasonic	Super EBA	96.8	Prospective
Rubinstein & Kim(2002)	91	5-7 y	59/91	Microscope	Ultrasonic	Super EBA	91.5	Prospective
Chong et al.(2003)	122	1-2 y	108/122	Microscope	Ultrasonic	MTA	92	Prospective
						IRM	87	
Taschieri et al.(2006)	80	1 y	71/80	Endoscope	Ultrasonic	EBA	94.9	RCT
				Loupe			90.6	
Tsesis et al.(2006)	110	>6 m	88/110	Microscope	Ultrasonic	IRM	91.1	Retrospective
				No aid	Bur		44.2	
Taschieri et al.(2007)	30	1 y	28/30	Endoscope	Ultrasonic	Super EBA	93	Prospective
Von Arx et al.(2007)	194	1 y	191/194	Endoscope	Sonic	MTA, Retroplast, Super EBA	83.8	Prospective
Von Arx et al.(2007)	183	1 y	177/183	Endoscope	Sonic	MTA, Super EBA	83	Prospective
Taschieri et al.(2008)	113	>2 y	100/113	Microscope	Ultrasonic	Super EBA	92	RCT
				Endoscope			90	
Saunder et al.(2008)	321	4-72 m	276/321	Microscope	Ultrasonic	MTA	88.8	Prospective
Kim et al.(2008)	263	1-5 y	192/263	Microscope	Ultrasonic	MTA, Super EBA	91.5	Prospective
Christiansen et al.(2009)	52	1 y	46/52	Microscope	Ultrasonic	MTA	96	RCT
						GP Smoothing	52	
Von Arx et al.(2010)	353	1 y	339/353	Microscope	Sonic	MTA	91.3	Prospective
						Retroplast	79.5	
Song et al.(2011)	54	1-7 y	42/54	Microscope	Ultrasonic	MTA, Super EBA	92.9	Prospective
Von Arx et al.(2012)	191	5y	170.191	Endoscope	Sonic	MTA, Retroplast, Super EBA	87.6	prospective
Song et al.(2012)	172	6-10y	104/172	Microscope	Ultrasonic	MTA, Super EBA	93.3	Prospective

MTA, Mineral Trioxide aggregate; IRM, Immediate Restorative Material; GP, gutta-percha

RCT, Randomized Controlled Trial study; m, month; y, year in intraoperative factors; apical and coronal seal in postoperative factors (Barone et al., 2010; Friedman, 2005; Lustmann et al., 1991; Rahbaran et al., 2001; von Arx et al., 2010). After microsurgical principles were introduced, the success rate of endodontic surgery was reported to be approximately 90% (Kim et al., 2008; Tsesis et al., 2009), which means that endodontic microsurgery has a considerably higher success rate than the traditional endodontic surgery. Because the surgical technique has become more precise and more predictable than the traditional endodontic surgery, the predictors affecting the clinical outcome of endodontic microsurgery might have changed and need to be re−investigated.

Von Arx et al. (von Arx et al., 2007a) evaluated the influence of various predictors on healing outcome 1 year after endodontic microsurgery with 194 teeth. With logistic regression, pain at initial examination ($P = 0.04$) was the only predictor reaching significance. In the study that assessed the 5−year outcome and its predictors in a cohort for which the 1−year outcome was reported, von Arx et al. (von Arx et al., 2012) revealed two significant outcome predictors; the mesial−distal bone level at ≤ 3 mm versus > 3 mm from the cementoenamel junction (78.2% vs 52.9%, $P < 0.02$) and root−end filling with ProRoot MTA versus Super EBA (86.4% vs 67.3%, $P < 0.004$). However, it is rare to report the prognostic factors on the endodontic microsurgery and more research is needed.

The endodontic surgery aims to remove the infected root end and ensure root canal sealing, while avoiding microleakage and penetration of bacteria and toxins from the tooth toward the periradicular tissues. So, root−end filling material with good sealing ability and biocompatibility is an important determinant for successful endodontic surgery (Gutmann and Harrison, 1991). For many years, amalgam has been accepted as the material of choice for root−end filling in endodontic surgery. However, with clear disadvantages of leakage and cytotoxicity, IRM and Super EBA have been suggested as alternative root−end filling materials to amalgam (Bondra et al., 1989; Dorn and Gartner, 1990). More recent studies have shown MTA to be a promising material for root−end filling. MTA has become popular because of several studies showing a good sealing ability and biocompatibility, and it has been attributed with the unique potential to induce or attach to the newly regenerating periodontal ligament (Al−Sa'eed et al., 2008; Maltezos et al., 2006; Torabinejad and Parirokh, 2010).

The search for a better root−end filling material has resulted in several clinical studies comparing IRM, Super EBA and MTA. Many clinical studies have shown nearly identical clinical outcomes with the use of IRM as with the use of MTA (Tsesis et al., 2006; Zuolo et al., 2000). In a randomized controlled study in endodontic microsurgery, Chong et al. (Chong et al., 2003) showed that the use of MTA as a root−end filling material resulted in a high success rate that was not significantly better than obtained using IRM. Super EBA has also resulted in a high success rate that is similar to MTA (Rubinstein and Kim, 2002; Taschieri et al., 2007). However, some experimental studies have shown that Super EBA is inferior to MTA with regards to microleakage and cytotoxicity (Maltezos et al., 2006; Osorio et al., 1998; Wu et al., 1998). Additional clinical study comparing Super EBA with MTA that provide more high level of evidence might also be needed.

Healing after endodontic surgery depends not only on hermetically sealing the root canal system via a retrograde approach but also on the hard tissue dimensions, ie, the deficiency of periapical and marginal bone tissue (Kim and Kratchman, 2006). In the studies of evaluating the healing outcome in relation to the preoperative lesion size measured radiographically, Wang et al. (Wang et al., 2004) and von Arx et al. (von Arx et al., 2007a) reported a better outcome in teeth with smaller ($\leq$ 5 mm) than with larger (5 > mm) lesions. With regard to the size of the bony crypt after bone preparation, positive correlation was found between larger periradicular defect size and unsuccessful or uncertain healing (Hirsch et al., 1979; Jansson et al., 1997). Especially for 'through and through' lesions, complete healing was only 25% (Hirsch et al., 1979).

A periodontally involved lesion also is believed to have an adverse effect on the outcome of apical surgery. Therefore, most studies on the outcome of endodontic surgery excluded those teeth presenting with an apicomarginal defect or a deep probing depth > 7 mm. Indeed, Kim et al. (Kim et al., 2008) suggested a poor prognosis for teeth with a periodontally involved lesion with a lower healing rate (77.5%) even though microscope-assisted regenerative technique was accompanied. When bony destruction of the pathological process includes a localized complete loss of marginal bone, the prognosis for success is reported to be 27% and 37% (Hirsch et al., 1979; Skoglund and Persson, 1985). The reason for the limited success has been identified as the formation of long junctional epithelium over the dehisced root surface (Rankow and Krasner, 1996).

With traditional endodontic surgery, there is a tendency to enlarge the osteotomy towards the coronal margin, away from the apex and root resection with steep bevel angle of 45 to 60 degree is inevitable. This results in excessive removal of healthy bone around the coronal root easily causing a periodontal-endodontic communication and interferes with the healing after surgery. However, the advantages of endodontic microsurgery include smaller osteotomies and shallower resection angles that conserve cortical bone and root length (Kim and Kratchman, 2006).

Therefore, this dissertation aims to examine the potential prognostic factors generally and investigate the effect of specific factors, root-end filling materials, and deficiency of periapical and marginal bone tissue, on the outcome of endodontic microsurgery. The first purpose of this study was to examine the potential prognostic factors on the outcome of endodontic microsurgery and compared the predictors of an isolated endodontic lesion with those of both an isolated endodontic lesion and endodontic−periodontal lesion retrospectively and prospectively. The second purpose was to evaluate the clinical outcomes of endodontic microsurgery when Super EBA and MTA were used as the root−end filling materials in a prospective randomized controlled study. And the last purpose was to assess the influence of deficiency of periapical and marginal bone tissue on clinical outcome after endodontic microsurgery.

II. Methods

This dissertation consists of four clinical studies – three cohort studies and a randomized controlled study (Fig 1).

Clinical data included in this study can be divided into retrospective and prospective data. Retrospective study included the data from the teeth performed endodontic microsurgery in the Microscope center of the Department of Conservative Dentistry at the Dental College, Yonsei University, Seoul, Korea between August 2004 and December 2008. Surgery was performed by 24 operators including 4 faculties and 20 residents. Retrospective study included some data of prospective study.

Data of prospective cohort study was accumulated by one operator (E.K.) from March 2001 to March 2011, which included the data of randomized controlled study on the root-end filling materials and the data of cohort study which assess the influence of deficiency of periapical and marginal bone tissue.

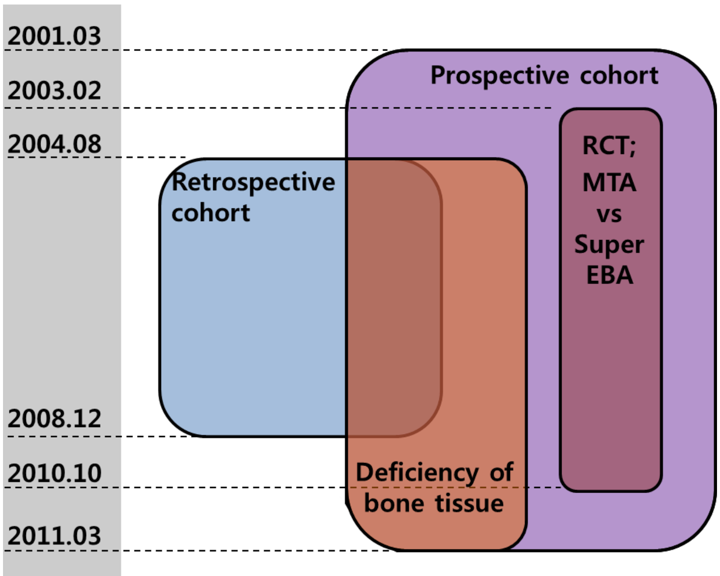

Figure 1. A schematic diagram showing the inclusion relationship of data

1-1. Prognostic factors in endodontic microsurgery: a retrospective cohort study

A. Case selection and inclusion/exclusion criteria

This study was approved by the University of Yonsei at Yonsei Dental College Institutional Review Board (IRB number 2004-2). The clinical database of the Microscope center of the Department of Conservative Dentistry at the Dental College, Yonsei University, Seoul, Korea, was searched for patients with a history of endodontic miscrosurgery performed between August 2004 and December 2008 and at least 1 year before being evaluated.

B. Surgical procedure

With the exception of the incisions, flap elevation, and suturing, all surgical procedures were performed using an operating microscope (OPMI PICO; Carl Zeiss, Göttingen, Germany). All clinical procedures were performed by endodontic faculties and residents.

After patients were anesthetized with 2% lidocaine with 1:80,000 epinephrine, sulcular or mucogingival incisions were chosen, depending on the type and aesthetic requirements of the case. For additional hemostasis during surgery, cotton pellets soaked in 0.1% epinephrine (Bosmin; Jeil Inc, Seoul, Korea) and/or ferric sulfate (Astringedent; Ultradent Products, Inc, South Jordan, UT) were applied topically as required. The tissue was gently reflected toward the apical area with a Molten 2-4 curette (G Hartzell and Son Inc, Concord, CA). In cases with mandibular second premolars or first molars, the mental foramen was identified by reflecting a vertical incision that was placed on the mesial to the first premolar. A KP1 retractor (G Hartzell and

Son Inc, Concord, CA) was then placed just coronal to the mental foramen, and a 1.5−cm−long and 2−mm−deep groove was made by using a #330 bur (Kim et al., 2001; Rahbaran et al., 2001). This groove was designed to protect the mental foramen during the surgical procedure by anchoring the serrated end of the retractor. Osteotomies were performed with a #4 round bur in an Impact Air 45 handpiece (Palisades Dental, Englewood, NJ). A Columbia 13-14 curette (G Hartzell and Son Inc) and a Jacquette 34/35 scaler (G Hartzell and Son Inc) were used for periradicular curettage. A 2−3mm root tip with a 0 to 10 degree bevel angle was sectioned with a chamfer diamond bur in an Impact Air 45 handpiece (Palisades Dental, Englewood, NJ) under copious sterile distilled water irrigation. The resected root surfaces were then stained with methylene blue and inspection with micromirror under 20 x to 26 x magnification to confirm the entire root tip resection and to search for other anatomic details overlooked. Root−end preparation extending 3 mm into the canal space along the long axis of the root were made with KIS ultrasonic tips (ObturaSpartan, Fenton, MO) driven by a piezoelectric ultrasonic unit (Spartan MTS; ObturaSpartan). Isthmuses, fins, and other significant anatomic irregularities were identified and treated with the ultrasonic instruments. After the root−end preparation is completed, the prepared cavity was also inspected with a micromirror at a high magnification (20 x to 26 x) to examine the cleanness of the root−end preparation. The prepared root end cavity was dried with a Stropko irrigator/drier (Obtura/Spartan). The root−end filling material used was an IRM (Caulk Dentsply, Milford, DE), Super EBA (Harry J. Bosworth, Skokie, IL), or ProRoot MTA (Dentsply, Tulsa, OK), which was selected according to the operators. The adaptation of the filling material to the canal apical walls was confirmed with the aid of an operating microscope at high magnification. The wound site was closed and sutured with 5x0 monofilament sutures, and a postoperative radiograph was taken to check for correct placement and an absence of excess material in the surgical site. A postoperative mouthwash

(0.2% chlorhexidine gluconate, Hexamedin; Bukwang Phar Co, Ansan, Korea) was commonly prescribed, and the sutures were removed 4 to 7 days later.

After surgery, an operation record form was made with the preoperative and intraoperative factors from the patient records and periapical radiographs. The operation record form was updated with the postoperative events whenever the patients were recalled periodically to assess the clinical and radiographic signs of healing.

C. Evaluation factors

The evaluation factors were divided into preoperative, intraoperative and postoperative factors. The preoperative factors included the patient's age and sex, tooth position, arch type, preoperative signs and/or symptoms, type of periapical radiolucency, root filling state (length, density, material), whether root canal treatment was the initial treatment or retreatment, history of apical surgery, presence or absence of post and restoration, and lesion type. Intraoperative factors included root−end filling material and operator. The postoperative factors included the presence or absence of a permanent restoration at follow−up.

The preoperative signs and/or symptoms were defined as preoperative pain or swelling, and the type of periapical radiolucency was divided into 3 subgroup, none (intact lamina dura), demarcated (well defined boundary) and diffuse (vague boundary). The adequate root filling length was defined as a filling within 2 mm from the apex, and the criteria of the adequate density was a filling without voids with uniform radiopacity. The lesion type was divided into isolated endodontic lesions (Class A, B, C) and endodontic−periodontal combined lesion (Class D, E, F), as classified by Kim and Kratchman (Kim and Kratchman, 2006). A large proportion of the data was collected mainly from the operation record form, and any missed record was referred to the patient records and periapical radiographs. If there was no postoperative record, the patients were contacted by telephone to attend a follow−up evaluation. Because all data in the operation record form was recorded by several operators, the factors evaluated from the radiographs were reevaluated and corrected by two examiners. These included the type of periapical radiolucency, root filling density and root filling length.

D. Clinical and radiographic evaluation

The patients were usually followed up at 3, 6 and 12 months and every year thereafter. On every recall visit, a routine examination was performed and periapical radiographs were taken. The clinical data including the signs and/or symptoms or loss of function, tenderness to percussion or palpation, subjective discomfort, mobility, sinus tract formation or periodontal pocket formation as well as postoperative complications, presence or absence of a restoration at follow−up were included in the operation record form.

The evaluation was performed at least 1 year after surgery. The postoperative radiographs were evaluated independently by two examiners using the same criteria employed by Molven et al. (Molven et al., 1987, 1996). The two examiners standardized the evaluation criteria before case analyses. Therefore, their results were based on the same evaluation methods and conditions. Cohen kappa statistical analysis was performed to measure the inter−examiner variability. Any disagreement regarding the clinical outcome was resolved by a discussion until agreement between the two examiners was reached. The radiographic healing classification was as follows: (i) complete healing, (ii) incomplete healing, (iii) uncertain healing, and (iv) unsatisfactory healing.

E. Assessment of outcome

Healing was judged clinically and radiographically. The criteria for a successful outcome included the absence of clinical signs and/or symptoms and radiographic evidence of complete or incomplete healing. The criteria for failure included any clinical signs and/or symptoms or radiographic evidence of uncertain or unsatisfactory healing.

F. Analyses of data

For statistical analysis of the predisposing factors, the dependent variable was the dichotomous outcome, success versus failure. A univariate description with the percentage frequencies was generated to characterize the study material. Significant associations between the outcome and all the variables were examined by bivariate analyses (x^2 or Fisher's exact tests) to identify the potential outcome predisposing factors. Multivariate analysis of the predisposing factors using Logistic Regression model was performed. All statistical analysis was two-tailed, performed with SPSS v19.0 software (IBM Corp, Somers, NY) and interpreted at the 5% level.

1-2. Prognostic factors in endodontic microsurgery: a prospective cohort study

A. Case selection and inclusion/exclusion criteria

This study was approved by the University of Yonsei at Yonsei Dental College Institutional Review Board (IRB number 2001-2), and informed consent was acquired from all participants. Data were collected from the Microscope center of the Department of Conservative Dentistry at the Dental College, Yonsei University, Seoul, Korea between March 2001 and March 2011. Teeth with mobility class II or greater, horizontal and vertical fractures, and perforation were excluded from the study. A total number of 584 teeth requiring endodontic surgery were included in the study.

B. Surgical procedure

All clinical procedures were the same as those cited in previous part (1-1.prognostic factors in endodontic microsurgery: a retrospective study) and were performed by a single operator (E.K.).

C. Evaluation factors

The evaluation factors were divided into preoperative, intraoperative and postoperative factors same as the retrospective study. The preoperative factors included the patient's age and sex, tooth position, arch type, preoperative signs and/or symptoms, probing depth, root filling state (length, density, material), whether root canal treatment was the initial treatment or retreatment, history of apical surgery, type of a preoperative restoration and lesion type. Intraoperative factors included root-end filling material, the presence or absence of complication and whether the tooth has a 'through and through' lesion. The postoperative factors included the type of a postoperative restoration at follow-up.

The preoperative signs and/or symptoms were defined as preoperative pain or swelling. The adequate root filling length was defined as a filling within 2mm from the apex, and the criteria of the adequate density was a filling without voids with uniform radiopacity. The lesion type was divided into isolated endodontic lesions (Class A, B, C) and endodontic-periodontal combined lesions (Class D, E, F), as classified by Kim and Kratchman (Kim and Kratchman, 2006). The type of preoperative and postoperative restoration was divided into 4 subgroup, single/splinted crown, short bridge, long bridge and RPD abutment. The resin core in the anterior teeth was included in the single/splinted crown. Short bridge was defined when the number of pontics are smaller than the number of abutments, on the contrary, long bridge was defined when the number of pontics are same or more than the number of abutments. The restoration of any type whatever, if that was used as abutment of removable partial denture (RPD), it was categorized as RPD abutment.

All data was recorded on the operation record form. Because on every recall visit, all data in the operation record form was updated by single doctor, the factors evaluated from the radiographs were reevaluated and corrected by two examiners. These included root filling density and root filling length.

D. Clinical and radiographic evaluation

The patients were usually followed up at 3, 6 and 12 months and every year thereafter and contacted by telephone to attend a follow-up evaluation. On every recall visit, a routine examination was performed and periapical radiographs were taken. The clinical data including the signs and/or symptoms or loss of function, tenderness to percussion or palpation, subjective discomfort, mobility, sinus tract formation or periodontal pocket formation as well as postoperative complications, type of a restoration at follow-up were included in the operation record form.

The evaluation was performed at least 1 year after surgery. The postoperative radiographs were evaluated independently by two examiners using the same criteria employed by Molven et al. (Molven et al., 1987, 1996) same as previous part – retrospective study.

E. Assessment of outcome

Healing was judged clinically and radiographically. The criteria for a successful outcome included the absence of clinical signs and/or symptoms and radiographic evidence of complete or incomplete healing. The criteria for failure included any clinical signs and/or symptoms or radiographic evidence of uncertain or unsatisfactory healing.

F. Analyses of data

For statistical analysis of the predisposing factors, the dependent variable was the dichotomous outcome, success versus failure. A univariate description with the percentage frequencies was generated to characterize the study material. Significant associations between the outcome and all the variables were examined by bivariate analyses (x^2 or Fisher's exact tests) to identify the potential outcome predisposing factors. Multivariate analysis of the predisposing factors using Logistic Regression model was performed. All statistical analysis was two-tailed, performed with SPSS v19.0 software (IBM Corp, Somers, NY) and interpreted at the 5% level.

2. MTA and Super EBA as root-end filling materials: a prospective randomized controlled study

A. Subject enrollment and inclusion/exclusion criteria

Approval for the project was obtained from the Yonsei University Committee for Research on Human Subjects (IRB number 2001-2), and informed consent was acquired from all participants. The study subjects were recruited from the pool of patients in the Microscope center of the Department of Conservative Dentistry at the Dental College, Yonsei University, Seoul, Korea, between February 2003 and October 2010.

All root-filled cases with symptomatic or asymptomatic apical periodontitis were included. Among them, teeth with class II mobility or greater, horizontal and vertical fractures, and perforations were excluded from the study. Through endodontic microsurgery, teeth with a through-and-through lesion and/or a lesion of combined periodontal endodontic origin were also excluded.

B. Sample size calculation

The sample size was determined with the method described by Walters (Walters, 2004) for comparing the means of ordinal data when the samples are presumed to display a relatively normal distribution. The anticipated success rate for MTA was expected to be 92% (Chong et al., 2003) and that of Super EBA was expected to be 85% (Testori et al., 1999). The minimum sample size was determined to be 281 on the basis of a 10% mean difference in outcome between the groups and power = 0.80 ($P < 0.05$). To ensure a minimum sample size of at least 140 subjects in each group at the 12-month follow-up examination, the goal was to enroll a total of 420 subjects, assuming that 20% of the patients might fail to attend and 20% of the patients might be excluded during surgery according to the exclusion criteria, such as the presence of a through-and-through lesion or a lesion of combined periodontal endodontic origin (Kim et al., 2008).

C. Sample size and randomization method

All patients were examined for inclusion in the study, and the clinical and radiographic examinations were undertaken. Of the 420 teeth confirmed to be eligible for endodontic microsurgery, 32 patients (32 teeth) chose not to participate. A total of 388 patients (388 teeth) met the inclusion criteria and consented to participate in the study. After written and verbal informed consent was obtained, endodontic microsurgery was performed. Of the 388 teeth on which endodontic microsurgery were performed, 16 teeth were excluded because of the presence of a through-and-through lesion, and 111 teeth were excluded because of the presence of a lesion with combined periodontal endodontic origin. One tooth that had insufficient depth of the root-end preparation because of the long post was also excluded. Excluding these 128 teeth, a total of 260 teeth were included in the randomized controlled trial (RCT), and they were randomly assigned to either the Super

EBA group or the MTA group (130 teeth per group) using the 'minimization method' as described by Pocock (Pocock, 1983). The random allocation sequence was generated by an assistant. The following 3 randomization factors were considered: sex, age, and tooth type.

D. Surgical procedure

All clinical procedures were the same as those cited in previous part (1-1.prognostic factors in endodontic microsurgery: a retrospective study) and were performed by a single operator (E.K.). The root-end filling material used was a Super EBA (Harry J. Bosworth, Skokie, IL), or ProRoot MTA (Dentsply, Tulsa, OK), which was selected according to randomization.

In the Super EBA group, the powder was slowly mixed into the liquid in small increments (in a 4:1 powder-to-liquid ratio) until a putty-like consistency was achieved. Then, the mixture was inserted incrementally into the dried cavity preparations and burnished. In the MTA group, white ProRoot MTA was mixed according to the manufacturer's directions (in a 3:1 powder-to-water ratio using sterile water) and incrementally placed into the root-end preparations.

E. Clinical and radiographic evaluation

The patients were followed up at 3, 6, and 12 months to assess the clinical and radiographic signs of healing. At every follow-up visit, a routine clinical and radiographic examination was performed. The primary outcome measure for this study was the change in the apical bone density at 12 months. The radiographic findings, which were taken from 3 angles (straight and 20 mesial and distal), were evaluated blindly and independently by 2 examiners using the same criteria used by Molven et al. (Molven et al., 1987, 1996). The healing classification was as follows (Molven et al., 1987, 1996) : (i) Complete healing, which was defined by the re-establishment of the lamina dura, (ii) Incomplete healing (scar tissue), (iii) Uncertain healing, (iv) Unsatisfactory healing.

The secondary outcome measures were the presence of clinical symptoms or abnormal findings at 12 months, such as any pain and/or swelling or loss of function, tenderness to percussion or palpation, subjective discomfort, mobility, sinus tract formation, or periodontal pocket formation. The 2 examiners standardized the evaluation criteria prior to the case analyses so that their results were based on the same evaluation methods and conditions. Cohen kappa statistical analysis was used to measure interexaminer variability. Disagreement regarding the clinical outcome was resolved by discussion until an agreement between the 2 examiners was reached.

F. Assessment of outcome

Success and failure were judged clinically and radiographically. The criteria for a successful outcome included the absence of clinical signs and symptoms and radiographic evidence of complete or incomplete healing. The criteria for failure included any clinical signs and/or symptoms or radiographic evidence of uncertain or unsatisfactory healing.

G. Statistical analysis

To analyze and compare the success rate according to the root−end filling material used (Super EBA vs MTA), a Pearson chi−square test was conducted with a significance level of 0.05 using SPSS v19.0 software (IBM Corp, Somers, NY).

3. Influence of deficiency of periapical and marginal bone tissue on clinical outcome: a prospective cohort study

A. Case selection and inclusion/exclusion criteria

Data were collected from the Microscope center of the Department of Conservative Dentistry at the Dental College, Yonsei University, Seoul, Korea between August 2004 and March 2011. Teeth with mobility class II or greater, horizontal and vertical fractures, and perforation were excluded from the study. Also, during the surgery, teeth that mucogingival incisions were chosen and teeth that bony crypts were connected across two or more roots were excluded. And teeth with apical crack were also excluded. A total number of 199 teeth requiring endodontic surgery were included in the study.

B. Surgical procedure

All clinical procedures were the same as those cited in previous part and were performed by a single operator (E.K.). Two root-end filling materials were chosen, Super EBA (Harry J. Bosworth, Skokie, IL), or ProRoot MTA (Dentsply, Tulsa, OK).

C. Evaluation parameters

During the surgical procedure, deficiencies of periapical and marginal bone tissue were measured just before the flap repositioned. The evaluation parameters were as follows: (A) Marginal bone loss: apicocoronal distance from cementoenamel junction or apical margin of restoration to marginal bone plate at mid-buccal site; (B) Height of buccal bone plate: apicocoronal distance of buccal bone plate covering root surface at mid-buccal site; (C) Width of bony crypt: greatest mesiodistal distance of bony crypt at the bone plate surface; (D) Height of bony crypt: greatest apicocoronal distance of bony crypt at the bone plate surface; (E) Depth of bony crypt: greatest distance of bony crypt measured from the bone plate surface to the lingual/palatal bone wall; and (F) approximate volume of bony crypt (C x D x E) (Fig 2).

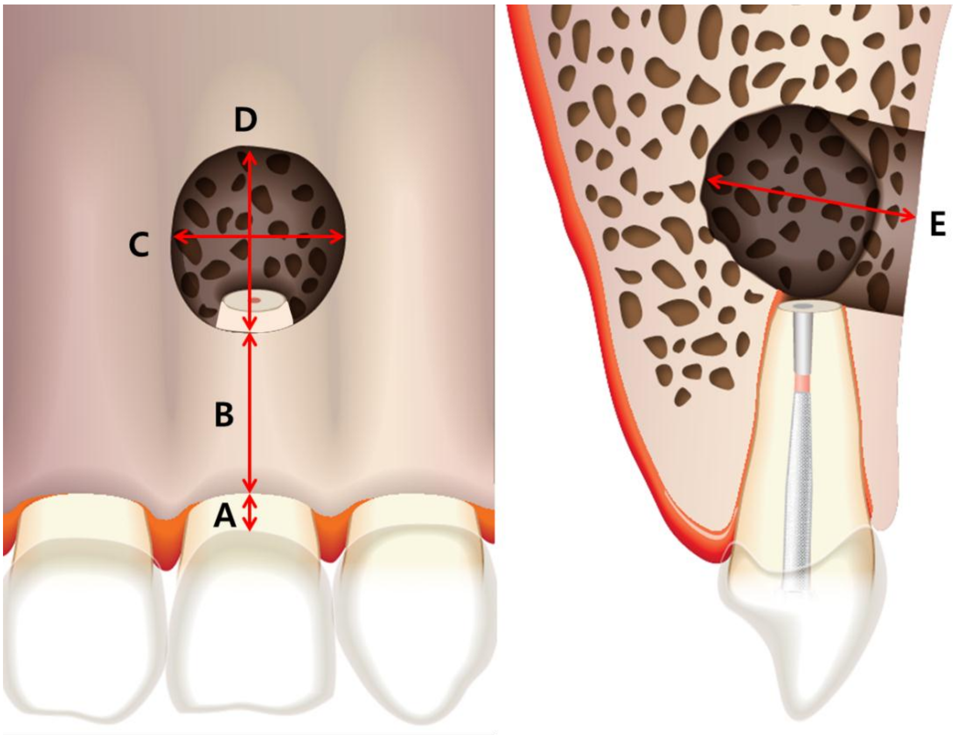

Figure 2. Schematic illustration of measurements taken intraoperatively. A. Marginal bone loss, B. Height of buccal bone plate, C. Width of bony crypt, D. Height of bony crypt, E. Depth of bony crypt

A single operator (E.K.) took all measurements, which were taken to the nearest 0.5mm with a periodontal probe (PCP10; Osung MND co., Korea). When the tooth had complete loss of buccal bone plate, marginal bone loss and height of buccal bone plate were not measured. And when the tooth presented with a 'through and through' lesion, depth of bony crypt was not measured. In case of marginal bone loss or height of buccal bone plate with a lot of difference in the mesial and distal, average were calculated with mesial and distal measurement.

D. Clinical and radiographic evaluation

The patients were usually followed up at 3, 6 and 12 months and every year thereafter. On every recall visit, a routine examination was performed and periapical radiographs were taken. The clinical data including the signs and/or symptoms or loss of function, tenderness to percussion or palpation, subjective discomfort, mobility, sinus tract formation or periodontal pocket formation as well as postoperative complications, presence or absence of a restoration at follow-up were included in the operation record form.

The evaluation was performed at least 1 year after surgery. The postoperative radiographs were evaluated independently by two examiners using the same criteria employed by Molven et al. (Molven et al., 1987, 1996). The two examiners standardized the evaluation criteria before case analyses. Therefore, their results were based on the same evaluation methods and conditions. Cohen kappa statistical analysis was performed to measure the inter-examiner variability. Any disagreement regarding the clinical outcome was resolved by a discussion until agreement between the two examiners was reached. The radiographic healing classification was as follows: (i) complete healing, (ii) incomplete healing, (iii) uncertain healing, and (iv) unsatisfactory healing.

E. Assessment of outcome

Healing was judged clinically and radiographically. The criteria for a successful outcome included the absence of clinical signs and/or symptoms and radiographic evidence of complete or incomplete healing. The criteria for failure included any clinical signs and/or symptoms or radiographic evidence of uncertain or unsatisfactory healing.

F. Analyses of data

With regard to the evaluated parameters, two sample t−test or Mann−Whitney U test were performed to find differences between the 2 groups (success versus failure) for all parameters. When marginal bone loss, height of buccal bone plate and depth of bony crypt were not measured, those were treated as missing data. In addition to these analyses, logistic regression model was performed with significant parameters which are assumed to be relevant clinically and statistically.

Ultimately, the present study aims to predict the healing outcome depending on the degree of deficiency of hard tissue rather than to compare the deficiency measurement depending on the healing outcome. Therefore, all measurements categorized. Each evaluation parameters has two subgroups, $\leq$ 5 mm and > 5 mm in width, height and depth of bony crypt; $\leq$ 3 mm and > 3 mm in marginal bone loss and height of buccal bone plate according to previous studies (von Arx et al., 2012, 2007b; Wang et al., 2004). Significant associations between the outcome and all the evaluation parameters were examined by a Pearson chi−square test or Fisher's exact test with a significance level of 0.05.

All statistical analyses were performed with SPSS v19.0 software (IBM Corp, Somers, NY).

III. Results

1-1. Prognostic factors in endodontic microsurgery: a retrospective study

Of the 907 cases with a history of endodontic microsurgery performed between August 2004 and December 2008, 491 were retained at follow-up. Table 2 and Table 3 lists the distribution of cases according to the variables/category and bivariate analysis. The Cohen kappa value for the preoperative type of periapical radiolucency, density, and length of pre-existing root filling as well as postoperative radiographs ranged from 0.83 to 0.94 (Table 4).

Of the preoperative factors examined, significant differences were observed for age ($P = 0.002$), sex ($P = 0.014$), tooth position ($P < 0.001$), root-filling length ($P = 0.020$), and lesion type ($P = 0.008$). Of the intraoperative factors, the root-end filling material ($P = 0.045$) was found to be significant. An evaluation of the restoration at follow-up revealed a higher success rate in the permanently restored group (85.3%) than the temporarily restored group (42.9%). This difference was also significant ($P = 0.012$).

Of the 491 cases recalled, 441 cases were related to an isolated endodontic lesion, and 50 cases were related to an endodontic periodontal combined lesion. With regard to the isolated endodontic lesion, the variables found to be significant were the tooth position ($P < 0.001$), root-filling length ($P = 0.016$), and restoration at follow-up ($P = 0.008$) (Table 3).

Table 2. Distribution of cases per variables/category and bivariate analysis

Variables/Category	Success N(%)	Failure N(%)	Chi-square value	P value
Age			18.900	**0.002**
<20	2(66.7)	1(33.3)		
21-30	90(90.9)	9(9.1)		
31-40	123(87.9)	17(12.1)		
41-50	66(81.5)	15(18.5)		
51-60	66(83.5)	13(16.5)		
>60	62(69.7)	27(30.3)		
Sex			6.068	**0.014**
Male	150(78.1)	42(21.9)		
Female	259(86.6)	40(13.4)		
Tooth position			16.648	**0.000**
Anterior	240(89.6)	28(10.4)		
Premolar	91(75.2)	30(24.8)		
Molar	78(76.5)	24(23.5)		
Arch type			0.000	0.990
Maxilla	299(83.3)	60(16.7)		
Mandible	110(83.3)	22(16.7)		
Right vs Left			0.118	0.731
Right	213(83.9)	41(16.1)		
Left	196(82.7)	41(17.3)		
Pre-op sign & symptom			0.056	0.814
No	33(84.6)	6(15.4)		
Yes	370(83.1)	75(16.9)		
Type of periapical radiolucency			1.405	0.495
None	29(85.3)	5(14.7)		
Demarcated	90(79.6)	23(20.4)		
Diffuse	289(84.3)	54(15.7)		
Root filling length			5.382	**0.020**
Adequate	171(79.5)	44(20.5)		
Inadequate	217(87.5)	31(12.5)		

Table 2. (Continued)

Variables/Category	Success N(%)	Failure N(%)	Chi-square value	P value
Root filling density			2.343	0.126
Adequate	185(81.1)	43(18.9)		
Inadequate	203(86.4)	32(13.6)		
Root filling material			2.892	0.235
Empty	21(80.8)	5(19.2)		
Gutta-percha	371(84.3)	69(15.7)		
Other	11(68.8)	5(31.3)		
Previous treatment			0.984	0.321
Initial	288(86.2)	46(13.8)		
Retreatment	68(81.9)	15(18.1)		
Previous apical surgery			0.867	0.352
No	358(84.0)	68(16.0)		
Yes	50(79.4)	13(20.6)		
Restoration			0.598	0.439
Permanent	340(82.7)	71(17.3)		
Temporary	69(86.3)	11(13.8)		
Post			0.422	0.516
Absent	264(82.5)	56(17.5)		
Present	145(84.8)	26(15.2)		
Lesion type			7.078	**0.008**
Endo	374(84.8)	67(15.2)		
Endo-perio	35(70.0)	15(30.0)		
Root-end filling material			6.191	**0.045**
MTA	214(85.6)	36(14.4)		
Super EBA	100(85.5)	17(14.5)		
IRM	83(75.5)	27(24.5)		
Operator			0.676	0.411
Faculty	357(83.8)	69(16.2)		
Resident	51(79.7)	13(20.3)		
Restoration at follow-up			9.576	**0.012**
Permanent	406(85.3)	70(14.7)		
Temporary	3(42.9)	4(57.1)		

Table 3. Distribution of cases per variables/category and bivariate analysis in isolated endodontic lesion

Variables/Category	Success N(%)	Failure N(%)	Chi-square value	P value
Age			10.349	0.066
<20	2(66.7)	1(33.3)		
21-30	82(90.1)	9(9.9)		
31-40	110(87.3)	16(12.7)		
41-50	64(85.3)	11(14.7)		
51-60	59(85.5)	10(14.5)		
>60	57(74.0)	20(26.0)		
Sex			2.111	0.146
Male	138(81.7)	31(18.3)		
Female	236(86.8)	36(13.2)		
Tooth position			16.685	**0.000**
Anterior	228(90.8)	23(9.2)		
Premolar	81(75.7)	26(24.3)		
Molar	65(78.3)	18(21.7)		
Arch type			0.090	0.764
Maxilla	280(85.1)	49(14.9)		
Mandible	94(83.9)	18(16.1)		
Right vs Left			0.226	0.634
Right	196(85.6)	33(14.4)		
Left	178(84.0)	34(16.0)		
Pre-op sign & symptom			0.011	0.917
No	32(84.2)	6(15.8)		
Yes	336(84.8)	60(15.2)		
Type of periapical radiolucency			0.999	0.607
None	26(86.7)	4(13.3)		
Demarcated	85(81.7)	19(18.3)		
Diffuse	262(85.6)	44(14.4)		
Root filling length			5.826	**0.016**
Adequate	154(80.6)	37(19.4)		
Inadequate	203(89.0)	25(11.0)		

Table 3. (Continued)

Variables/Category	Success N(%)	Failure N(%)	Chi-square value	P value
Root filling density			3.260	0.071
Adequate	163(81.9)	36(18.1)		
Inadequate	194(88.2)	26(11.8)		
Root filling material			4.176	0.124
Empty	19(79.2)	5(20.8)		
Gutta-percha	341(85.9)	56(14.1)		
Other	11(68.8)	5(31.3)		
Previous treatment			0.468	0.494
Initial	267(87.5)	38(12.5)		
Retreatment	60(84.5)	11(15.5)		
Previous apical surgery			0.179	0.672
No	329(85.2)	57(14.8)		
Yes	44(83.0)	9(17.0)		
Restoration			0.114	0.736
Permanent	312(84.6)	57(15.4)		
Temporary	62(86.1)	10(13.9)		
Post			0.120	0.729
Absent	243(84.4)	45(15.6)		
Present	131(85.6)	22(14.4)		
Root-end filling material			3.090	0.213
MTA	186(86.9)	28(13.1)		
Super EBA	95(85.6)	16(14.4)		
IRM	81(79.4)	21(20.6)		
Operator			0.519	0.471
Faculty	324(85.3)	56(14.7)		
Resident	49(81.7)	11(18.3)		
Restoration at follow-up			11.206	**0.008**
Permanent	371(86.9)	56(13.1)		
Temporary	3(42.9)	4(57.1)		

Table 4. Interexaminer reliability in evaluating preoperative and postoperative radiographs

Factors	Agreement (%)	Cohen's kappa value
Periapical radiolucency type	97.59	0.88
Root filling density	92.07	0.84
Root filling length	91.67	0.83
Postoperative radiographs	98.96	0.94

Table 5. Logistic regression model (total)

Variables	Point Estimate	95% Confidence Interval		P value
		Lower	Upper	
Sex				
Female versus male	1.789	1.031	3.104	**0.039**
Tooth position				
Anterior versus premolar	2.888	1.527	5.463	**0.001**
Anterior versus molar	2.349	1.128	4.890	**0.022**
Root filling length				
Inadequate versus adequate	1.684	0.965	2.938	0.066
Lesion type				
Endo versus endo-perio	2.566	1.183	5.564	**0.017**
Root-end filling material				
MTA versus Super EBA	1.978	0.962	4.067	0.064
MTA versus IRM	2.417	1.251	4.668	**0.009**
Permanent restoration at follow up				
Yes versus no	4.597	0.630	33.546	0.133

Endo, isolated endodontic lesion; Endo+perio, Both isolated endodontic lesion and endodontic-periodontal lesion.

The coefficient of determination, 0.134

For logistic regression, an almost−full model was considered first. The nonsignificant predictors for R^2, such as age, root−filling material, and density, were excluded. Table 5 lists the point estimate, 95% confidence intervals of the odds ratios, and the P value of the significant remaining parameters. Sex (female), tooth position (anterior), lesion type (endodontic lesion), and root−end filling material (MTA and Super EBA) were found to have a positive effect on the outcome (Table 5). On the other hand, with the isolated endodontic lesion, only the tooth position (anterior) was significant (Table 6).

Table 6. Logistic regression model (isolated endodontic lesion)

Variables	Point Estimate	95% Confidence Interval		P value
		Lower	Upper	
Sex				
Female versus male	1.345	0.730	2.476	0.341
Tooth position				
Anterior versus premolar	3.524	1.785	6.960	**0.000**
Anterior versus molar	2.303	1.013	5.232	**0.046**
Root filling length				
Inadequate versus adequate	1.818	0.982	3.366	0.057
Lesion type				
A versus B	2.239	0.628	7.986	0.214
A versus C	2.198	0.589	8.199	0.241
Root-end filling material				
MTA versus Super EBA	1.877	0.885	3.984	0.101
MTA versus IRM	1.837	0.893	3.782	0.099
Permanent restoration at follow up				
Yes versus no	4.008	0.554	28.984	0.169

The coefficient of determination, 0.112

1-2. Prognostic factors in endodontic microsurgery: a prospective study

Of the 584 cases treated, 431 cases came for recall after a period of at least 12 months. A recall rate of 73.8% (431/584) was obtained and Table 7 presents the distribution of cases in relation to the recall period. Table 8 and Table 9 list the distribution of cases according to the variables/category and bivariate analysis. The Cohen kappa value for density and length of pre-existing root filling as well as postoperative radiographs ranged from 0.87 to 0.95 (Table 10).

Table 7. Distribution of cases related to recall period

Recall period	No. of teeth (%)
1 year	110 (18.8)
2 years	120 (20.7)
3 years	40 (6.8)
4 years	37 (6.3)
5 years	18 (3.1)
6 years	27 (4.6)
7 years	23 (3.9)
8 years	30 (5.1)
9 years	23 (3.9)
10 years	3 (0.5)

Of the preoperative factors examined, significant differences were observed for age ($P < 0.001$), sex ($P = 0.027$), tooth position ($P = 0.002$), arch type ($P = 0.002$), and lesion type ($P = 0.001$). Of the intraoperative and postoperative factors, none was found to be significant ($P > 0.05$).

Table 8. Distribution of cases per variables/category and bivariate analysis

Variables/Category	Success N(%)	Failure N(%)	Chi-square value	P value
Age			30.529	**0.000**
<20	15(100.0)	0(0.0)		
21-30	87(92.6)	7(7.4)		
31-40	108(92.3)	9(7.7)		
41-50	67(78.8)	18(21.2)		
51-60	63(86.3)	10(13.7)		
>60	29(61.7)	16(38.3)		
Sex			4.860	**0.027**
Male	136(81.0)	32(19.0)		
Female	233(88.6)	30(11.4)		
Tooth position			12.487	**0.002**
Anterior	208(91.2)	20(8.8)		
Premolar	69(80.2)	17(19.8)		
Molar	92(78.6)	25(21.4)		
Arch type			9.183	**0.002**
Maxilla	272(88.9)	34(11.1)		
Mandible	97(77.6)	28(22.4)		
Right vs Left			0.993	0.334
Right	155(87.6)	22(12.4)		
Left	214(84.3)	40(15.7)		
Pre-op sign & symptom			0.019	0.890
No	50(86.2)	8(13.8)		
Yes	319(85.5)	54(14.5)		
Probing depth			2.580	0.275
≤4mm	305(86.9)	46(13.1)		
5-7mm	30(78.9)	8(21.1)		
≥8mm	34(81.0)	8(19.0)		
Root filling length			3.641	0.056
Adequate	172(83.5)	34(16.5)		
Inadequate	149(90.3)	16(9.7)		

Table 8. (Continued)

Variables/Category	Success N(%)	Failure N(%)	Chi-square value	P value
Root filling density			1.923	0.166
Adequate	185(84.5)	34(15.5)		
Inadequate	136(89.5)	16(10.5)		
Root filling material			0.410	0.921
Empty	36(87.8)	5(12.2)		
Gutta-percha	280(86.4)	44(13.6)		
Other	5(83.3)	1(16.7)		
Previous treatment			0.054	0.816
Initial	272(86.3)	43(13.7)		
Retreatment	49(87.5)	7(12.5)		
Previous apical surgery			1.968	0.161
No	322(86.6)	50(13.4)		
Yes	47(79.7)	12(20.3)		
Preoperative restoration type			4.322	0.208
Single, splinted crown	311(85.4)	53(14.6)		
Short bridge	31(93.9)	2(6.1)		
Long bridge	13(72.2)	5(27.8)		
RPD abutment	14(87.5)	2(12.5)		
Lesion type			10.520	**0.001**
Endo	304(88.4)	40(11.6)		
Endo-perio	65(74.7)	22(25.3)		
Root-end filling material			0.327	0.835
MTA	167(85.2)	29(14.8)		
Super EBA	192(86.1)	31(13.9)		
IRM	10(83.3)	2(16.7)		
Complication				
Absence	354(85.5)	60(14.5)		1.000
Presence	15(88.2)	2(11.8)		
Through & through lesion				1.000
No	347(85.5)	59(14.5)		
Yes	22(88.0)	3(12.0)		

Table 8. (Continued)

Variables/Category	Success N(%)	Failure N(%)	Chi-square value	P value
Postoperative restoration type			4.322	0.208
Single, splinted crown	311(85.4)	53(14.6)		
Short bridge	31(93.9)	2(6.1)		
Long bridge	13(72.2)	5(27.8)		
RPD abutment	14(87.5)	2(12.5)		

Of the 431cases recalled, 344 cases were related to an isolated endodontic lesion, and 87 cases were related to an endodontic-periodontal combined lesion. With regard to the isolated endodontic lesion, the variables found to be significant were the age (P = 0.005), tooth position (P = 0.006), and arch type (P = 0.002) in the preoperative factors. And type of postoperative restoration (P = 0.023) was also found to be significant (Table 9).

Table 9. Distribution of cases per variables/category and bivariate analysis in isolated endodontic lesion

Variables/Category	Success N(%)	Failure N(%)	Chi-square value	P value
Age			16.067	**0.005**
<20	13(100.0)	0(0.0)		
21-30	67(93.1)	5(6.9)		
31-40	90(94.7)	5(5.3)		
41-50	60(83.3)	12(16.7)		
51-60	47(85.5)	8(14.5)		
>60	27(73.0)	10(27.0)		
Sex			0.605	0.437
Male	110(86.6)	17(13.4)		
Female	194(89.4)	23(10.6)		
Tooth position			10.342	**0.006**
Anterior	180(93.3)	13(6.7)		
Premolar	54(83.1)	11(16.9)		
Molar	70(81.4)	16(18.6)		

Table 9. (Continued)

Variables/Category	Success N(%)	Failure N(%)	Chi-square value	P value
Tooth position			10.342	**0.006**
Anterior	180(93.3)	13(6.7)		
Premolar	54(83.1)	11(16.9)		
Molar	70(81.4)	16(18.6)		
Arch type			9.610	**0.002**
Maxilla	230(91.6)	21(8.4)		
Mandible	74(79.6)	19(20.4)		
Right vs Left			0.531	0.466
Right	126(86.9)	19(13.1)		
Left	178(89.4)	21(10.6)		
Pre-op sign & symptom			0.080	0.778
No	43(89.6)	5(10.4)		
Yes	261(88.2)	35(11.8)		
Probing depth			1.436	0.529
≤4mm	273(88.6)	35(11.4)		
5-7mm	24(88.9)	3(11.1)		
≥8mm	7(77.8)	2(22.2)		
Root filling length			0.160	0.689
Adequate	145(88.4)	19(11.6)		
Inadequate	124(89.9)	14(10.1)		
Root filling density			0.102	0.750
Adequate	147(88.6)	19(11.4)		
Inadequate	122(89.7)	14(10.3)		
Root filling material			0.668	0.726
Empty	30(85.7)	5(14.3)		
Gutta-percha	235(89.4)	28(10.6)		
Other	4(100.0)	0(0.0)		
Previous treatment				0.781
Initial	234(88.6)	30(11.4)		
Retreatment	35(92.1)	3(7.9)		

Table 9. (Continued)

Variables/Category	Success N(%)	Failure N(%)	Chi-square value	P value
Previous apical surgery				0.295
No	270(89.1)	33(10.9)		
Yes	34(82.9)	7(17.1)		
Preoperative restoration type			6.728	0.053
Single, splinted crown	256(88.3)	34(11.7)		
Short bridge	25(100.0)	0(0.0)		
Long bridge	12(75.0)	4(25.0)		
RPD abutment	11(84.6)	2(15.4)		
Lesion type			1.274	0.529
A	45(91.8)	4(8.2)		
B	161(89.0)	20(11.0)		
C	98(86.0)	16(14.0)		
Root-end filling material			0.894	0.616
MTA	135(90.0)	15(10.0)		
Super EBA	162(87.1)	24(12.9)		
IRM	7(87.5)	1(12.5)		
Complication				1.000
Absence	292(88.2)	39(11.8)		
Presence	12(92.3)	1(7.7)		
Through & through lesion				1.000
No	285(88.2)	38(11.8)		
Yes	19(90.5)	2(9.5)		
Postoperative restoration type			8.730	**0.023**
Single, splinted crown	247(87.9)	34(12.1)		
Short bridge	34(100.0)	0(0.0)		
Long bridge	12(75.0)	4(25.0)		
RPD abutment	11(84.6)	2(15.4)		

Table 10. Interexaminer reliability in evaluating preoperative and postoperative radiographs

Factors	Agreement (%)	Cohen's kappa value
Root filling density	97.57	0.95
Root filling length	96.23	0.92
Postoperative radiographs	97.22	0.87

Minimizing the number of variables in logistic regression makes the better model. Referred to the previous results of retrospective study, variables with significance level of 0.05 or less are included. Table 11 and 12 lists the point estimate, 95% confidence intervals of the odds ratios, and the P value of the significant remaining parameters. Sex (female), tooth position (anterior), arch type (maxilla), lesion type (endodontic lesion) were found to have a positive effect on the outcome (Table 11).

Table 11. Logistic regression model (total)

Variables	Point Estimate	95% Confidence Interval		P value
		Lower	Upper	
Sex				
Female versus male	1.926	1.090	3.403	**0.024**
Tooth position				
Anterior versus premolar	2.176	1.057	4.479	**0.035**
Anterior versus molar	2.288	1.154	4.537	**0.018**
Arch type				
Maxilla versus mandible	1.922	1.059	3.485	**0.032**
Lesion type				
Endo versus endo-perio	2.061	1.120	3.793	**0.020**

Endo, isolated endodontic lesion; Endo+perio, Both isolated endodontic lesion and endodontic-periodontal lesion.

The coefficient of determination, 0.115

On the other hand, with the isolated endodontic lesion, the tooth position (anterior) and arch type (maxilla) was significant (Table 12). And type of postoperative restoration (long bridge) was found to have a negative effect on the outcome (P = 0.022).

Table 12. Logistic regression model (isolated endodontic lesion)

Variables	Point Estimate	95% Confidence Interval		P value
		Lower	Upper	
Sex				
Female versus male	1.489	0.733	3.027	0.271
Tooth position				
Anterior versus premolar	3.060	1.210	7.739	**0.018**
Anterior versus molar	3.445	1.407	8.437	**0.007**
Arch type				
Maxilla versus mandible	2.118	1.024	4.381	**0.043**
Postoperative restoration type				
Single versus short bridge	0.000	0.000	0.000	0.998
Single versus long bridge	4.653	1.246	17.382	**0.022**
Single versus RPD abutment	1.330	0.253	6.976	0.736

The coefficient of determination, 0.157

2. A prospective randomized controlled study of MTA and Super EBA as root−end filling materials

Among the 260 teeth included in this randomized controlled trial, 192 teeth were examined at the 12−month follow−up. A total of 102 were examined from the Super EBA group, 90 teeth were examined from the MTA group, and 68 teeth were lost to follow−up.

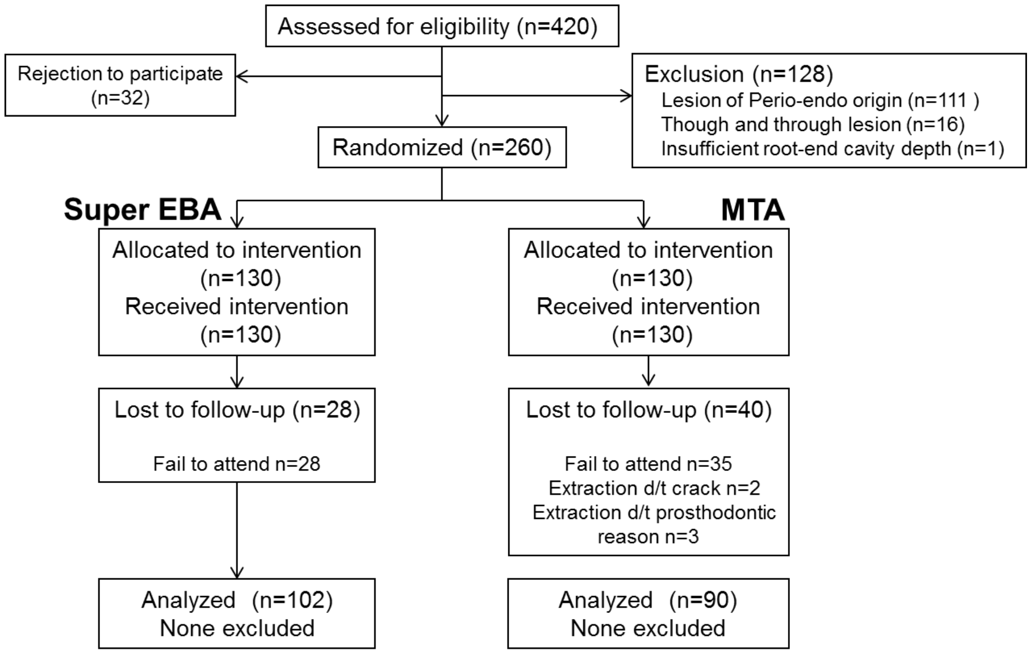

Figure 3. A flow diagram of subject's progress through the phases of a randomized trial.

The reasons for drop out are given in Figure 3. Table 13 lists the distribution of the analyzed cases according to the root−end filling material used.

The overall success rate was 94.3%, with a success rate of 95.6% (86/90 teeth) for MTA and 93.1% (95/102 teeth) for Super EBA. The statistical analysis of the success rate results did not show any significant difference between the groups (P = 0.472). The categorization of the treatment outcome according to the clinical and radiographic parameters is shown in Table 14. The Cohen kappa value was 0.91, which shows that the agreement between the 2 examiners was high.

Table 13. Distribution of analyzed cases per root−end filling material used

	Super EBA(n=102) (53.1%)		MTA(n=90) (46.9%)		Total(n=192) (100%)	
	N	%	N	%	N	%
Sex						
Male	35	34.3	34	37.8	69	35.9
Female	67	65.7	56	62.2	123	64.1
Age						
<20	5	4.9	2	2.2	7	3.6
20-29	23	22.5	18	20.0	41	21.4
30-39	24	23.5	35	38.9	59	30.7
40-49	15	14.7	15	16.7	30	15.6
50-59	21	20.6	13	14.4	34	17.7
>60	14	13.7	7	7.8	21	10.9
Tooth type						
Maxillary anterior	41	40.2	32	35.6	73	38.0
Premolar	18	17.6	13	14.4	31	16.1
Molar	14	13.7	14	15.6	28	14.6
Mandibular anterior	9	8.8	12	13.3	21	10.9
Premolar	6	5.9	5	5.6	11	5.7
Molar	14	13.7	14	15.6	28	14.6

Table 14. Summary of treatment outcome by combined radiologic and clinical criteria per root−end filling material used

Category of healing	Super EBA (n=102)		MTA (n=90)		Total (n=192)	
	N	%	N	%	N	%
Complete healing	74	72.5	69	76.7	143	74.5
Incomplete healing	21	20.6	17	18.9	38	19.8
Uncertain healing	4	3.9	0	0	4	2.1
Unsatisfactory healing	3	2.9	4	4.4	7	3.6

3. Influence of deficiency of marginal and periapical bone tissue on clinical outcome

Of the 199 cases treated, 135 cases came for recall a period of 12 months at least. A recall rate of 67.8% (135 of 199 teeth) was obtained and overall success rate was 85.2% (115 of 135 teeth). Table 15 lists the distribution of analyzed cases according to the age, sex and tooth position. Table 16 presents the distribution of cases in relation to the recall period. The kappa value was 0.81, which shows the agreement between the 2 examiners was very good.

Table 15. Distribution of cases

Variables	No. of teeth
Age (y)	
<20	8
21-30	34
31-40	29
41-50	28
51-60	23
>60	13
Sex	
Male	55
Female	80
Tooth position	
Maxillary, anterior	38
Premolar	28
Molar	25
Mandibular, anterior	11
Premolar	8
Molar	25

Table 16. Distribution of cases related to recall period

Recall period	No. of teeth(%)
1 year	41 (30.4)
2 years	51 (37.8)
3 years	16 (11.9)
4 years	18 (13.3)
5 years	4 (3.0)
6 years	2 (1.5)
7 years	3 (2.2)

Of the 135 analyzed, 7 teeth present a through and through lesion and 27 teeth has complete loss of buccal bone plate. Measurements of each parameter were presented in table 17, no significant difference was found for the parameters in success versus failure cases (P > 0.05).

Table 17. Measurement and p value of parameters taken during surgery

Evaluation parameter	Success		Failure		P value
	N	Mean±SD(mm)	N	Mean±SD(mm)	
(A) Marginal bone loss	96	2.6±1.0	12	3.0±1.2	0.214
(B) Height of buccal bone plate	96	4.7±1.8	12	3.8±2.3	0.113
	N	**Median±IQR(mm)**	**N**	**Median±IQR(mm)**	
(C) Width of bony crypt	115	6.0±1.0	20	5.5±1.0	0.330
(D) Height of bony crypt	115	6.0±3.0	20	6.0±3.5	0.620
(E) Depth of bony crypt	74	7.5±3.0	10	8.0±3.8	0.989
(F) Volume of bony crypt	74	279.0±204.0	10	285.0±216.0	0.415

SD, standard deviation; IQR, inter-quartile range

Logistic regression model was performed with significant parameters which are assumed to be relevant clinically and statistically (Table 18). This model included variables with significance level of 0.30 or less and volume of bony crypt.

Table 18. Logistic regression for significance of measured parameters

Variables	Point Estimate	95% Confidence Interval		P value
		Lower	Upper	
(A) Marginal bone loss	1.748	0.770	3.968	0.181
(B) Height of buccal bone plate	0.555	0.316	0.974	**0.040**
(F) Volume of bony crypt	0.998	0.989	1.006	0.586

The coefficient of determination, 0.246

The logistic regression model showed only 1 parameter which is the height of buccal bone plate proved to be significant (P = 0.040).

Pearson chi-square test was consistent with the result of logistic regression. With regard to the periapical bone tissue, the statistical analysis of the success rate depending on the diameter of bony crypt or a 'through and through' lesion did not show any significant differences (Table 19). However, absence or presence of buccal bone plate is potential predictors of the healing outcome, teeth with complete loss of buccal bone plate showed lower healing rate than those which are not (70.4% vs 88.9%, P = 0.029). And teeth with the buccal bone plate with > 3 mm showed a higher success rate than teeth with ≤ 3 mm (94.3% vs 66.7%, P = 0.002). Marginal bone loss did not significantly impact the healing outcome.

Table 19. Distribution of cases per variables/category and bivariate analysis

Variables/category	Success N(%)	Failure N(%)	Chi-square value	P value
Through and through lesion				1.000
Yes	6 (85.7)	1(14.3)		
No	109 (85.2)	19 (14.8)		
Width of bony crypt			0.105	0.746
≤5mm	53 (84.1)	10 (15.9)		
>5mm	62 (86.1)	10 (13.9)		
Height of bony crypt			0.508	0.476
≤5mm	38 (88.4)	5 (11.6)		
>5mm	77 (83.7)	15 (16.3)		
Depth of bony crypt				1.000
≤5mm	14 (87.5)	2 (12.5)		
>5mm	60 (88.2)	8 (11.8)		
Complete loss of buccal bone plate				**0.029**
Yes	19 (70.4)	8 (29.6)		
No	96 (88.9)	12 (11.1)		
Marginal bone loss				1.000
≤3mm	67 (89.3)	8 (10.7)		
>3mm	29 (87.9)	4 (12.1)		
Height of buccal bone plate				**0.002**
≤3mm	14 (66.7)	7 (33.3)		
>3mm	82 (94.3)	5 (5.7)		

IV. Discussion

Many studies reported that microorganism in the root canals or periradicular lesions play a major role in the persistence of apical periodontitis (Gomes et al., 2008; Lin et al., 1992; Sundqvist et al., 1998). By inspection of the root apex and resected root surface during endodontic microsurgery, we examined the clinical causes of failure and the limitation of previous endodontic treatment (Song et al., 2011). With the results, the most common possible cause of failure was perceived leakage around the canal filling material (30.4%), followed by a missing canal (19.7%), underfilling (14.2%), anatomical complexity (8.7%), overfilling (3.0%), iatrogenic problems (2.8%), apical calculus (1.8%), and cracks (1.2%) (Fig. 4).

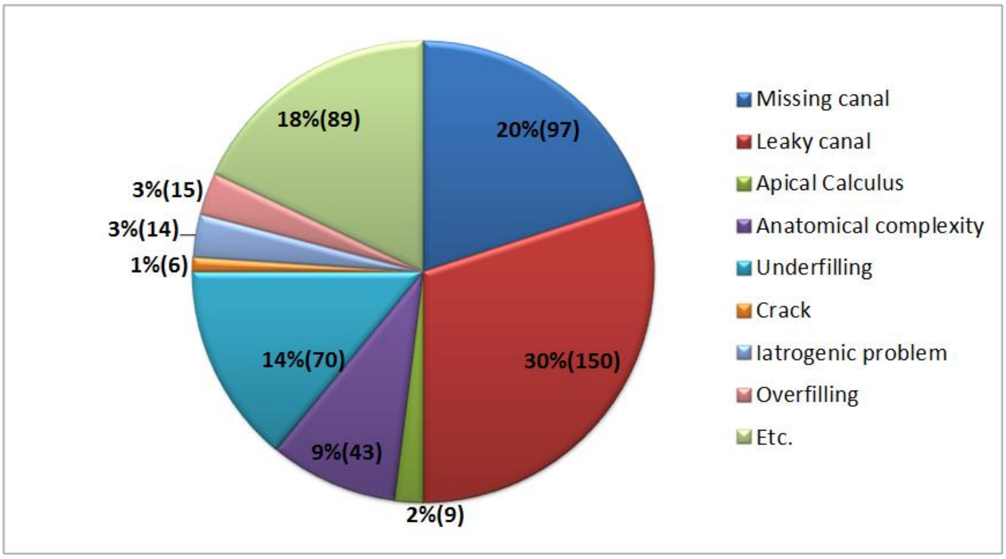

Figure 4. Percentage (N) of the possible causes of failure in previous root canal treatment. (Song et al., 2011)

Failure by missing canal, underfilling and overfilling can be reduced by understanding the root canal anatomy of the tooth type and using the microscope and ultrasonic devices. However, some parts of the causes such as leakage or anatomical complexity caused by the porous tubular structure of dentin and canal irregularities or a limitation of materials might be difficult to resolve with nonsurgical endodontic treatment.

Endodontic surgery can solve the many problems which nonsurgical treatment cannot resolve, and surgical intervention might be the last resort before the tooth extraction. In endodontic surgery, the prognostic factors should be considered for the case selection, if we know. In addition, it is helpful to weigh the endodontic surgery against alternative treatments if we can predict the treatment outcome. Therefore, there has been a continuous effort to examine the prognostic factors and to find the materials and techniques for higher success rate. This dissertation also designed for the same purpose but intended to distinguish from the existing many other studies by dealing with the endodontic microsurgery only using ultrasonic root-end preparation, biocompatible root-end filling materials and high-power illumination and magnification (10 x and higher).

1. Prognostic factors in endodontic microsurgery: cohort studies

Well-designed cohort studies offer a clear and appropriate temporal sequence from exposure to outcome, providing strong support for causation (Torabinejad and Bahjri, 2005). This cohort study examined the predictors retrospectively and prospectively, that were discussed with respect to the specific data reported in the literature along with the preoperative factors that have received the most attention. Retrospective studies are subject to various forms of bias that may distort their conclusions. Because most of the data depend on previous records, which were obtained by each operator before the study was designed, bias can occur at the stage of case selection as well as during the evaluation of the preoperative and postoperative factors.

In this retrospective study, all evaluation also relied on the operation record form and it cannot be sure that surgical procedures were performed under control. An attempt was made to compensate for this limitation with a re-evaluation of the pre- and postoperative radiographs by two examiners, and very good kappa values were obtained. Moreover, on the contrary to the prospective study of which procedure was performed by single operator, several operators participated in the retrospective study. It provided the effect of operator for clinical outcomes and makes the result be generalized.

Retrospective study and prospective study used almost same evaluation factors and showed similar results. This study showed that several factors, such as sex, tooth position, lesion type, root-end filling material, and type of postoperative restoration, have a significant effect on the healing outcome of endodontic microsurgery but failed to show a difference between previously reported studies dealing with traditional apical surgery and the present study dealing with endodontic microsurgery. Nevertheless, it is likely that preoperative factors, particularly the tooth position and arch type, have a higher weight on the healing outcome than intra- and postoperative factors.

Age

In many studies, the patient's age and sex have no significant effect on the treatment outcome (Rubinstein and Kim, 1999; Wang et al., 2004; Zuolo et al., 2000). In the present study, various healing outcomes were observed according to the age group and sex ($P < 0.05$). The highest success rate was reported in patients in their 20s, 30s and tended to decrease as the patients aged. Generally, younger patients have a better healing potential. However, a longer follow-up could make this difference weak.

Sex

This study showed males had a poorer success rate than females. In the periodontal literature, it has been shown that males are more prone to periodontal infection than females (Desvarieux et al., 2004). In an endodontic outcome study (Marquis et al., 2006), it was shown that male patients had a significantly lower success rate of initial root canal treatment when compared with female patients. And also, in the experimental study with mice of pathologic endodontic bone loss, the increase in inflammatory infiltrate correlates to more bone loss in the male mice (McAbee et al., 2012). However, the clinical significance of sexual dimorphism in periapical inflammation and wound healing has not been fully elucidated.

Healing aspect according to sex might be related with systemic disease and smoking. In 2006 review paper, Duncan and Pitt Ford (Duncan and Pitt Ford, 2006) demonstrated a paucity of evidence relating smoking with endodontic disease and prognosis, but nevertheless present evidence of a likely increase in surgical complications. As well as impairing hard tissue healing and soft tissue healing (Castillo et al., 2005; Chang et al., 1996; W−Dahl and Toksvig−Larsen, 2004), smoking is likely to affect healing in surgical endodontic cases that involve bony and soft tissue healing. The present study did not include smoking habit as evaluation factor, therefore, definite correlation between healing and smoking habit or sex was not revealed. Further studies would be needed to assess the relation between them.

Tooth position

The anterior teeth, the premolar and molar teeth had a significantly different success rate of microsurgery ($P < 0.05$). In this prospective study, significant difference also was observed between the maxillary and mandibular groups ($P < 0.05$). The anterior teeth tended to have a higher success rate than the other tooth groups (Kim and Kratchman, 2006), which might be caused by the specific convenience of access and the root anatomy (Friedman, 1998). Indeed, the use of an operating microscope does not enhance access (Kim and Kratchman, 2006), positioning of surgeons and patients for posterior and/or mandibular teeth is not as convenient as that of anterior and/or maxillary teeth.

Preoperative signs and/or symptoms

In the present study, the preoperative signs and/or symptoms did not influence the outcome of endodontic microsurgery, even though von Arx et al. (von Arx et al., 2007) reported that pain at the initial examination was the only significant predictor. Endodontic microsurgery with transillumination and magnification might completely eradicate the source of reinfection regardless of the tooth status.

Preoperative canal filling state (length, density and material)

The root-filling status preoperatively can be characterized by the material, density, and length. The root-filling materials and density does not affect the outcome of microsurgery (Barone et al., 2010; Rahbaran et al., 2001). However, effect of the root-filling length on the outcome of microsurgery showed diverse. In the present retrospective study, after defining an adequate length as a filling within 2 mm from the apex, teeth with an inadequate root-filling length showed a significantly higher success rate than those with an adequate root-filling length ($P = 0.020$). However, logistic regression model showed that root-filling length was not significant ($P = 0.066$). Barone et al. (Barone et al., 2010) also reported that a preoperative root-filling length has a significant effect. The unfilled portion of the root canal in the short root fillings might be the main infected site, and the extruded portion beyond the root end may help with persistent disease. Because these are resected during the surgical procedure, the surgical approach will enable a successful outcome in inadequately root-filled teeth

(Farzaneh et al., 2004; Lustmann et al., 1991). However, in the present prospective study, root-filling length did not demonstrate any significant influence on the healing outcome ($P > 0.05$) along with von Arx et al. (von Arx et al., 2007) and Jensen et al. (Jensen et al., 2002). A periapical radiograph limited to a two-dimensional picture only cannot provide the real information about root-filling length and density, so preoperative canal filling state evaluated radiographically might be unsuitable for evaluation factors.

Previous treatment (initial or retreatment)

There were no significant differences in the previous endodontic treatment, initial treatment, or retreatment ($P > 0.05$). With traditional endodontic surgery, the surgical approach to seal the bacteria within the canal might be ineffective. Therefore, the outcome of endodontic surgery for previously treated teeth might be compromised. On the other hand, according to the microsurgical principles with a microscope, biocompatible materials can seal off all potential routes of microbial escape from the root canal system within the follow-up period (Song et al., 2011).

Previous apical surgery

Many studies reported that resurgery has a very poor success rate compared with the initial endodontic surgery (Gagliani et al., 2005; von Arx et al., 2010). However, this study did not show any significant difference on the outcome regarding the history of previous apical surgery. A previous study (Song et al., 2011) reported that the causes of failure of the first endodontic surgery were related to an incomplete surgical technique such as no root end filling and incorrect root end preparation (Fig 5). Therefore, the use of a microsurgical technique resulted in a high clinical success rate even in endodontic resurgery. Wang et al. (Wang et al., 2004) suggested that the modified case selection and techniques may have been responsible for their higher healing rate after resurgery than in previous studies.

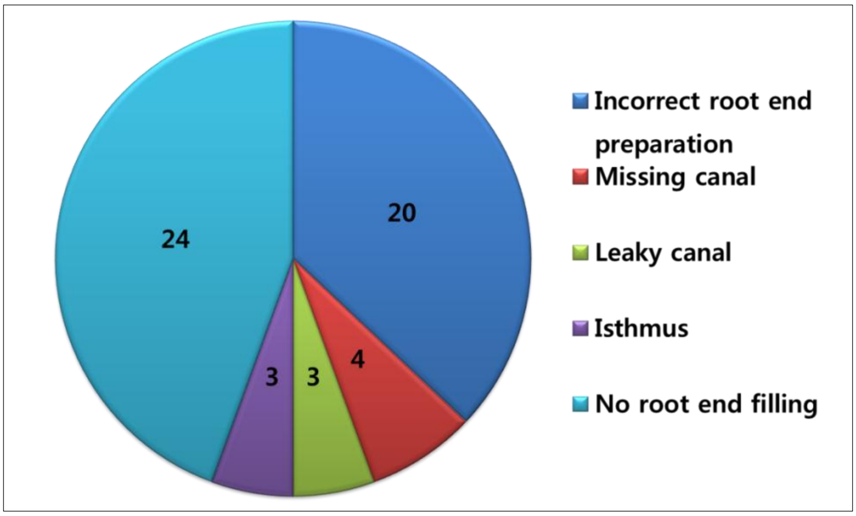

Figure 5. Possible causes of failure in previous surgery. (Song et al., 2011)

Lesion type

A periodontally involved lesion is believed to have an adverse effect on the outcome of apical surgery. Therefore, most studies evaluating the potential prognostic factors for the healing outcome in apical surgery excluded those teeth presenting with an apicomarginal defect or a deep probing depth ≥ 7 mm(von Arx et al., 2007; Zuolo et al., 2000). Indeed, some studies suggested a poor prognosis for teeth with a periodontally involved lesion with a lower healing rate (Hirsch et al., 1979; Kim et al., 2008; Wang et al., 2004). In the present retrospective and prospective study, the lesion type is a significant predictor (retrospective study, $P = 0.008$; prospective study, $P = 0.001$).

In previous studies, the intraoperative factors included many items related to the technical procedure, such as the level of apical resection, degree of beveling, presence/absence of a root−end filling, method of root−end preparation, root−end filling depth, magnification, and illumination (Barone et al., 2010; Friedman, 2005). However, the potential confounding effects of multiple variables increased with the increasing number of variables. This makes an analysis of the effect of different variables on the prognosis more complex, which may lead to different conclusions. The surgical procedures in the present study were performed under the strict manual of microsurgical techniques regardless of the operators. Endodontic microsurgery uses a dental operating microscope to allow a more precise procedure with little or no bevel of the root end resection and root-end preparation with the aid of an ultrasonic tip to a depth of 3 to 4 mm (Rubinstein and Kim, 1999). It provides a predictable treatment with a much higher success rate (Tsesis et al., 2009) and reduces the various intraoperative factors affecting the outcome.

Root-end filling material

The effect of a root-end filling material is the most commonly studied factor among the intraoperative factors. Recently, biocompatible materials, such as IRM, Super EBA, and MTA, have been used with the microsurgical technique. Two randomized controlled trials comparing MTA with IRM cement in periapical endodontic surgery showed no significant differences (Chong et al., 2003; Lindeboom et al., 2005). In vitro studies comparing MTA with Super EBA reported similar results of periapical bone regeneration and the leakage test (Baek et al., 2010; Pichardo et al., 2006). Moreover, a prospective clinical study evaluating the outcomes of microsurgery showed no significant differences between MTA and Super EBA (Kim et al., 2008). In this prospective study, root-end filling materials does not affect the outcome of microsurgery ($P = 0.835$). More detailed discussion regarding MTA and Super EBA as a root-end filling material will be described in the later. On the other hand, in this retrospective study, there were only significant differences for the root-end filling material between IRM and MTA (logistic regression, $P = 0.009$). Eugenol leaching from the IRM may reduce the healing potential, and moisture in the surgical procedure can reduce the sealing ability of the IRM (Dorn and Gartner, 1990).

Operator

The effects of the operator skill have received less attention. It is normally assumed that faculties with considerable experience have a higher success rate than residents. Lustmann et al. (Lustmann et al., 1991) reported that even if there were significant differences between the operators, the classification of the surgeon according to the number of years in practice proved to be irrelevant. On the other hand, one study reported that teeth treated by postgraduate dental students had a significantly higher survival probability than those treated by staff, which was attributed to case selection (Wang et al., 2004). In this retrospective study, no significant differences were observed between the healing outcome of the faculties and residents. Residents in Yonsei are trained under the supervision of faculty with a strict manual of endodontic microsurgery from the second year, and third year residents are fully experienced. Therefore, it is natural that that success rate of residents would be comparable to that of faculty. In the prospective study, a single operator performed all clinical procedure, so effect of operators could not be evaluated.

Through and through lesion

In this prospective study, teeth with a through and through lesion did not demonstrate any significant influence on the healing outcome ($P > 0.05$). However, in general, presence of the intact lingual/palatal wall might be considered to affect the healing outcome (Pecora et al., 2001; Tsesis et al., 2011). Even though this prospective cohort has been accumulated for more than 10 years, the total number of teeth with a through and through was only 25, thus, additional studies with more cases will be needed to provide a high level of evidence.

Postoperative restoration

With regard to the coronal seal, Rahbaran et al. (Rahbaran et al., 2001) reported that a tooth with a good coronal restoration had three times the odds of having complete periapical healing than that without a restoration. Rapp et al. (Rapp et al., 1991) hypothesized that the likelihood of complete healing was greater when a permanent restoration was present. On the other hand, one study with an assessment of the 4- to 10-year outcome of apical surgery, prospectively, concluded that the restoration at follow-up had no significant healing rate differential (Barone et al., 2010). In this retrospective study, the healing outcome was related to the restoration at follow-up. On the other hand, under the control of some variables, the restoration had no significant influence at follow-up (logistic regression, $P = 0.133$). The possibility of reinfection from an insufficient crown restoration might be compensated for by the tight seal of the root-end filling. With regard to the type of restoration, this prospective study showed no significant differences between types of preoperative and postoperative restoration ($P = 0.208$).

Although endodontic periodontally involved teeth are in the endodontic domain, the prognosis of the teeth depends on the periodontal support and endodontic microsurgical treatment (Dietrich et al., 2003). Therefore, the predisposing factors of an isolated endodontic lesion after endodontic microsurgery would be different from those of an endodontic periodontally involved lesion. With the isolated endodontic lesion, the tooth position, root-filling length, and restoration at follow-up were significant at the 95% confidence level in the retrospective study. And age, the tooth position, arch type, and type of postoperative restoration were in the prospective study. However, under the control of some variables, the tooth position (anterior) was the only predictor reaching significance under the control of significant factors (logistic regression, $P < 0.05$) in the retrospective study, and in the prospective study, additional factors such as arch type and type of postoperative restoration were the predictors (logistic regression, $P < 0.05$).

In the present prospective study, teeth restored with long bridge showed lower healing rate than teeth restored with single/splinted crown, short bridge and RPD abutment (logistic regression, $P = 0.022$). Long bridge was defined when the number of pontics are same or more than the number of abutment. In the fixed prosthodontics with several pontics, the ability of the abutment teeth to accept applied forces is important for prognosis (Rosenstiel et al., 2006). The tooth performed with endodontic microsurgery has shorter root more than 3 mm, it can lead an unfavorable outcome considering the Ante's law that it was unwise to provide a fixed prosthodontics when the root surface area of the abutment was less than the root surface area of the teeth being replaced (Shillingburg et al.). Also, under the overloading of abutment with long span, root−end filling materials might be hard to bear the occlusal pressure.

In conclusion, the potential prognostic factors on the outcome include sex, tooth position, arch type, lesion type, and root−end filling material. An isolated endodontic lesion might reduce the effect of many variables in the outcome of endodontic microsurgery, the tooth position, arch type and type of restoration were found to be a pure predictor of an endodontic lesion affecting the clinical outcome, even though the logistic regression model has small coefficient of the determination (retrospective analysis: 0.112, prospective analysis: 0.157) (Nagelkerke, 1991).

2. A prospective randomized controlled study of MTA and Super EBA as root−end filling materials

Both MTA and Super EBA are considered suitable retrograde filling materials and have been shown to possess biocompatibility and good apical sealing properties (Dorn and Gartner, 1990; Torabinejad and Parirokh, 2010). However, some in vitro and ex vivo studies comparing MTA with Super EBA showed that Super EBA is inferior to MTA (Maltezos et al., 2006; Osorio et al., 1998; Wu et al., 1998). In a fluid filtration model, Wu et al (Wu et al., 1998) noted an increase in microleakage with Super EBA (from 0% to 55%) and a decrease in microleakage with MTA (from 55% to 0%) from 24 hours to 3 months. An in vitro bacterial leakage model, which is more clinically relevant than models using dyes or isotopes, showed that MTA leaked significantly less than Super EBA (Maltezos et al., 2006). The superiority of MTA is more remarkable because of its biocompatible properties. Osorio et al. (Osorio et al., 1998) showed that from the different materials tested, all materials were cytotoxic except MTA. In their study, MTA showed no cytotoxicity in any test system. Conversely, Super EBA was the only material that was cytotoxic in a cell viability test (Al−Sa'eed et al., 2008). Samara et al found that MTA does not inhibit cell growth and adherence in the human periodontal ligament (Samara et al., 2011). Furthermore, Baek et al. (Baek et al., 2010) observed bone regeneration and cementum−like tissue formation over MTA.

Even though many experimental studies have reported that MTA is superior to Super EBA, there was no statistical significance in the healing outcome between Super EBA and MTA in the present study. Studies using extracted teeth or a simulated model in vitro setting are easier to perform and allow for a more objective evaluation of the effectiveness of a material in terms of apical sealing, leakage, marginal adaptation, biocompatibility, and cytotoxicity (Yin et al., 2010). However, these studies are performed under conditions that differ from those found in actual surgical practice. Therefore, they cannot reflect the influence of the clinical conditions. Moreover, the human body has a natural ability to heal mild inflammation and adapt to foreign materials. If a certain amount of toxicity can be tolerated and the inferior properties of Super EBA can be compensated by the host responses, there is no impact on the clinical outcome of surgery. Therefore, it should be taken into consideration that experimental studies cannot provide conclusive determination of the results of clinical application, and direct application of the results of experimental studies to a clinical setting is risk laden (Niederman and Theodosopoulou, 2003; Yin et al., 2010).

In the present study, the clinical and radiographic examination at 12 months was used as the outcome measure. Although peak healing occurs in the first year after surgery, it has been reported that a reversal to a disease state may occur in apparently healed cases within 4 years after treatment (Halse et al., 1991; Jesslen et al., 1995; Rubinstein and Kim, 2002). Friedman (Friedman, 2011) suggested that the long-term outcomes might not be as good as the short-term outcomes. However, the most significant information regarding healing was obtained 1 year after surgery, and a transition of inadequately healed teeth 1 year after surgery to completely healed teeth after 5 or 6 years has also been reported in some studies (Halse et al., 1991; Jesslen et al., 1995). Therefore, some prospective studies on the clinical outcomes of surgical endodontics have reported outcomes after follow-up periods of approximately 1 year (Chong et al., 2003; Taschieri et al., 2007). In addition, we followed up the cases that were classified as healed at the short term follow-up for an additional 6 to 10 years and reported a high maintained success rate of 93.3% based on the long-term follow-up (Song et al., 2012), which is consistent with the general consensus.

Studies on the clinical outcomes require a precise definition of the inclusion/exclusion criteria considering the confounding variables, and such studies run the risk of losing patients at follow-up, which makes it difficult to recruit and allocate the patients. A sufficient sample size was planned for the present study to identify differences between the 2 groups. Based on a previous study (Kim et al., 2008), we speculated that approximately 20% of the teeth requiring endodontic microsurgery represented teeth with a lesion of combined periodontal endodontic origin and/or a through-and-through lesion. However, 33% (160 teeth) of the total teeth were excluded during surgery, and only 260 teeth were included in the study, which was less than expected. In addition, we calculated the sample size on the basis of an expected 10% mean difference in the outcome between the MTA and the Super EBA groups. However, the difference in the outcome between the 2 groups in the present study was below 5%. To detect a subtle difference in the outcome between the groups, a larger sample size would be needed.

Despite the limitations, the strength of the present study is that randomization with regard to the root-end filling materials was performed, and the checklist of items to include when reporting a randomized trial and the participant flow diagram (Fig 3) were followed to reveal the strengths and limitations of the study (Moher et al., 2005). In any randomized trial, it is desirable that the treatment groups should be similar regarding the relevant prognostic factors. Based on preliminary studies (prognostic factors in endodontic microsurgery), sex, age, and tooth type were found to be potential prognostic factors for the clinical outcome. To balance the marginal treatment totals for each level of each prognostic factor, the Pocock minimization method was used. The randomization procedure seemed to be adequate because the clinical variables, which could have an impact on healing, were equally distributed between the 2 groups. The results can be influenced by many unknown and uncontrolled variables. In the present study, however, the number of teeth in each group was reasonably evenly distributed by sex, age, and tooth type, which might reduce a significant source of bias.

RCTs have advantages, such as a comparative study design, which play a critical role in the identification of the best treatment method. Additionally, the randomization procedure minimizes or removes an uneven distribution of known and unknown confounding factors that can influence the clinical outcome between groups. In addition, the blinding procedure used in RCTs prevents observers from preferring one treatment over another, and the researchers can control the study's exposure level (Torabinejad and Bahjri, 2005). Well-controlled RCTs, which are frequently referred to as the 'gold standard' of research, can provide the strongest evidence of causation (Oleckno, 2002). However, because of the strict eligibility criteria and loss to follow-up, the sample size requirements for a RCT are difficult to attain and maintain, and this eventually results in limited validity of results. Therefore, to raise the power of the evidence, meta-analysis with similarly designed RCTs can be a way to provide more practical and reliable recommendations for clinical practice.

In conclusion, in this prospective randomized controlled study, there was no significant difference in the clinical outcomes of endodontic microsurgery when Super EBA and MTA were used as root-end filling materials. However, because of the scarcity of randomized clinical trials comparing Super EBA with MTA directly, additional studies will be needed to provide a high level of evidence regarding root-end filling materials.

3. Influence of deficiency of marginal and periapical bone tissue on clinical outcome

With endodontic microsurgery, von Arx et al. (von Arx et al., 2007b) assessed the influence of bone defect dimensions on healing outcome. He failed to show any relationship between the level and height of the buccal bone plate and healing outcome 1 year after apical surgery. In contrast, the size of the bony crypt was correlated with healing at follow-up; non-healed cases presented larger width of bony crypts at the time of apical surgery than healed cases. The difference from the present study was teeth presenting with tunnel lesions and teeth with complete loss of facial bone plate had been excluded.

In the present study, all teeth with a 'through and through' lesion or complete loss of buccal bone plate were included to confirm the effect on the healing outcome. In order to remove the bias due to the surgical procedure, any additional regenerative techniques were not performed in all cases. It might be the reason of the 85.2% success rate in this study, which is lower than that of other studies on the healing outcome of endodontic microsurgery (Kim et al., 2008; Setzer et al., 2010). In this study, the deficiency of bone tissue on the healing outcome was evaluated periapically and marginally. Unlike von Arx et al. (von Arx et al., 2007b), deficiency of marginal bone tissue became more important predictors on outcome than deficiency of periapical bone tissue in this study.

Many studies reported that a less extensive periapcial bony destruction had a tendency to better healing (von Arx et al., 2007b; Wang et al., 2004). Complete periapical wound healing after endodontic surgery includes regeneration of alveolar bone, periodontal ligament, and cementum (Lin et al., 2010). In order for this to happen, periosteum plays a very important role as a source of osteo−competent cells and as a barrier against the penetration of epithelial cells into the healing sites (Pecora et al., 2001). In case of large bony defects and 'through and through' lesions where both cortical bone plates are lost, however, the periosteum is likely to be damaged by the infective process. Consequently, extensive periapcial bony destruction tends to be healed by fibrous connective tissue repair (Tsesis et al., 2011) and the required time to complete healing appears to need more (Jansson et al., 1997).

In the present study, there was no difference in healing outcome between the teeth with size (width, height and depth) of bony crypt > 5 mm and ≤ 5 mm (P > 0.05). And teeth with presenting a 'through and through' lesion also had apparently the same frequency of success as the teeth with intact lingual/palatal wall. This result might stem from the way of the evaluation; dichotomized healing outcome (success versus failure). Success group included incomplete healing as well as complete healing, which is evaluated not histologically but clinically and radiographically. Therefore, even though histological complete healing was not achieved, clinically, it can be regarded as success. And in the present study, teeth with presenting a 'through and through' lesion were only 8 cases, which weakened the statistical power.

With regard of deficiency of marginal bone tissue, teeth with complete loss of buccal bone plate showed 70.4% success rate, which is lower than that of teeth with intact buccal bone plate (P = 0.029). In the teeth with buccal dehiscence, the PDL and cementum are destroyed, which is hard to prevent apical migration of junctional epithelium along the denuded root surface into the periapical wound and to induce selective repopulation of cells of the connective tissue attachment (Lin et al., 2010). Whereas the isolated endodontic lesion is primarily a closed wound, dehiscence is mostly open wound and a dissemination of the marginal inflammation to the apical area might be easy to take place (Tsesis et al., 2011). It is the explanation for teeth with apicomarginal defect to show lower healing outcome.

In case of teeth with buccal bone plate, height of buccal bone was associated with the healing outcome ($P = 0.040$). Wang et al. (Wang et al., 2004), who identify actors that might affect the survival of teeth after endodontic surgery, reported that teeth with less than 4mm peroperative marginal bone loss from the cementoenamel junction had a significantly longer survival time than those with more than 4mm marginal bone loss preoperatively ($P < 0.03$). And von Arx (von Arx et al., 2012) also demonstrated that mesial-distal crestal bone level at ≤ 3 mm versus > 3 mm from the cementoenamel junction is statistically significant predictor of a healing outcome (78.2% vs 52.9%, $P < 0.02$). However, in the present study, there is no significant difference between the teeth with marginal bone loss ≤ 3 mm and > 3 mm (89.3% and 87.9%, $P = 1.000$). On the other hand, teeth with height of buccal bone plate less than 3mm had a significantly lower success rate than those with more than 3mm height of buccal bone plate (66.7% vs 94.3%, $P = 0.002$). It might be a tendency of increase in the marginal bone loss with reduction of the height of buccal bone plate. But it was not necessarily inversely proportional because root length is not fixed, and in this study, there was no correlation between the two variables. Therefore, only height of buccal bone plate showed statistical significance regardless of marginal bone loss.

Wesson and Gale (Wesson and Gale, 2003), who evaluated molar apicectomies, reported that the depth of the buccal/palatal 'bone cuff' prior to closure are shown in relation to the 5 year healing outcome after surgery. Successful healing was found in 76% of teeth with a bone cuff of 3 mm or greater but only 55% of teeth with a bone cuff of 2 mm and only 47% of teeth with a bone cuff of 1 mm ($P < 0.0001$). One must consider that a thin buccal bone plate might be resorbed as a result of the mere reflection of a full-thickness flap or as a result of drying out of the denuded bone tissue (Harrison and Jurosky, 1991). Therefore, considering the consecutive resorption and resistance to the pathologic change of marginal bone, teeth should be secured the buccal bone plate with at least 3 mm or more. A osteotomy towards the apical margin away from the crown and root resection with minimal bevel angle is helpful to conserve the bone tissue especially in case of Asian, whose root length were shorter than those of Caucasians (Kim et al., 2005).

This study showed that the deficiency of marginal bone tissue has a significant effect on the healing outcome of endodontic microsurgery, similar to the many previous studies on endodontic surgery. However, this study showed the height of buccal bone plate is only predictor of healing outcome, not marginal bone loss. So, when teeth are covered with buccal bone plate more than 3mm, the marginal bone loss does not affect on the healing outcome. Loss of the buccal cortex might be due to marginal periodontitis or might result from anatomic dehiscence caused by prominent roots and surgical procedure such as osteotomy. If dehiscence is naturally occurring, a fibrous connective attachment is present between the root surfaces and the mucosa. However, if the cause of dehiscence is pathologic as a result of marginal periodontitis, regenerative technique is suggested to improve the healing outcome after endodontic surgery with preventing apical migration of junctional epithelium along the root surfaces (Oh et al., 2009).

V. Conclusion

Within some limitations of this study, the potential positive prognostic factors on the outcome include sex (female), tooth position (anterior), arch type (maxilla), lesion type (isolated endodontic lesion), and root-end filling material (MTA and Super EBA). An isolated endodontic lesion might reduce the effect of many variables in the outcome of endodontic microsurgery, the tooth position (anterior), arch type (maxilla) and type of restoration (single/splinted crown, short bridge and RPD abutment) were found to be a pure positive predictor of an endodontic lesion affecting the clinical outcome.

In this prospective randomized controlled study to investigate the effect of root-end filling materials, there was no significant difference in the clinical outcomes of endodontic microsurgery when Super EBA and MTA were used as root-end filling materials.

With assessment of the influence of deficiency of marginal and periapical bone tissue on clinical outcome, the height of buccal bone plate (more than 3 mm) was only a positive predictor of healing outcome.

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국문요약

미세 치근단 수술의 예후인자에 대한 연구: 세 개의 코호트 연구와 하나의 무작위 배정 연구

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송민주

본 논문은 미세치근단 수술의 전반적인 예후인자를 알아보고, 역충전 재료와 치근단 및 치경부 골결손 정도와 같은 특정 요소가 수술의 예후에 미치는 영향을 알아보고자 한다.

1. 미세치근단 수술의 예후인자: 후향적 코호트 연구와 전향적 코호트 연구

이번 연구의 목적은 전향적, 후향적 연구 설계를 통해 미세치근단 수술의 예후인자를 알아보고 치주-치수 복합 병소를 포함한 전체 수술 증례에서의 예후인자와 독립된 치수 병소를 가진 증례만 분석하여 얻은 예후인자를 비교해보고자 함이다.

후향적 연구를 위해 2004년 8월부터 2008년 12월까지 미세치근단 수술을 받은 치아 중 최소 1년 이상 관찰된 치아의 자료만을 수집했다. 전향적 연구에서는 2001년 3월부터 2011년 3월까지 미세치근단 수술을 받은 584개의 치아를 대상으로 했다. 수술 후에는 수술기록지에 임상, 방사선 검사를 통해 얻어진 술전, 술 중, 술 후 요소를 기록하였고 통계분석을 위해 예후는 성공, 실패로 이분화시켰다.

그 결과, 성별(여자), 치아 위치(전치부), 악골 위치(상악), 병소유형(독립 치수병소), 역충전 재료(MTA, Super EBA)가 결과에 긍정적인 예후인자로 나타났다. 독립된 치수병소만을 분석한 경우, 결과에 영향을 주는 변수의 수를 줄일 수 있었고 치아 위치(전치부), 악골 위치(상악), 술후 수복물 형태(크라운/연결된 크라운, 짧은 브릿지, 국소의치의 지대치)가 예후에 긍정적인 영향을 주는 것으로 나타났다.

2. 역충전 재료로서 MTA와 Super EBA가 예후에 미치는 영향: 무작위 배정 연구 (RCT)

두 번째 목적은 무작위 배정 연구 설계를 통해 MTA와 Super EBA를 역충전 재료로 사용했을 때 미세치근단 수술의 예후를 평가하고자 하였다.

미세치근단 수술이 필요한 388개 치아 중에 128개를 제외한 260개의 치아만이 연구에 포함되었고 "minimization method"를 이용하여 MTA군과 Super EBA군에 동일한 수로 배정되었다. 수술 술식은 이전 연구와 동일하게 Yonsei protocol을 따랐으며 한 명의 술자가 진행하였다. 환자는 3개월, 6개월, 12개월 후 평가를 시행하였다. 첫 번째 평가 기준은 술 후 12개월의 치근단의 방사선 밀도이고 두 번째 평가 기준은 술 후 12개월의 임상 증상 및 이상 소견 여부였다.

총 192개의 치아가 술 후 12개월에 평가되었고 Super EBA군 102개, MTA 군 90개였다. 전체 성공률은 94.3%였고, 각각 MTA 95.6%(86/90), Super EBA 93.1%(95/102)였다. 통계분석 결과, 두 재료는 성공률에 있어 유의한 차이를 갖지 않았다 ($P = 0.472$).

3. 치근단 및 치경부 골조직 결손이 예후에 미치는 영향: 전향적 코호트 연구

마지막 목적은 치근단 및 치경부 골조직 결손이 미세치근단 수술의 결과에 미치는 영향을 평가하는 것이다.

2004년 8월에서 2011년 3월 사이 치근단 수술이 필요한 199개의 치아가 포함되었다. 술식을 시행하고 마지막 피판을 재위치시키기 직전에 치근단 및 치경부 골조직 결손 정도를 측정하였다. 성공한 증례와 실패한 증례에서 각각의 평가항목이 수치가 차이가 나는지 t-test 혹은 Mann Whitney U test를 통해 분석해보고,

임상적, 통계적으로 유의한 변수를 가지고 로지스틱 회귀분석도 시행하였다. 마지막으로 각 변수를 특정 수치를 기준으로 범주화하여 $x2$ test를 통해 상관관계를 알아보았다.

소환률은 67.8%(135/199)였고 성공률은 85.2%였다. 협측골판의 유무가 치유의 예측인자로 나타났고, 협측골판이 완전히 소실된 경우, 그렇지 않은 경우보다 낮은 성공률을 보였다(70.4% vs 88.9%, P = 0.029). 그리고 잔존 협측골의 폭이 3 mm보다 큰 경우가 3 mm 이하인 경우보다 높은 성공률을 보였다 (94.3% vs 66.7%, P = 0.002).

미세치근단 수술에 영향을 미치는 요소는 다양하다. 그러나 표준화된 술식을 정립함으로써 그 영향을 주는 요소를 줄일 수 있다. 성별, 치주상태, 치아 위치와 같은 환자-치아 관련 요소가 예후인자로 나타났고, 역충전재료와 술후 수복물 형태 또한 예후인자로 고려할 수 있었다. 그러나 이에 관련한 연구가 부족하므로 이번 연구 결과를 뒷받침하기 위해서는 더 많은 전향적 코호트 연구 및 RCT연구가 필요하다.

핵심 되는 말: 미세치근단 수술, 치근단절제술, 임상 연구, 무작위 배정 연구, 예후인자, 임상 결과, mineral trioxide aggregate(MTA), super ethoxy-benzoic acid(Super EBA), 골결손, 치경부 골결손, 협측골판

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