Ph.D. Thesis

Evaluation of panoramic radiographic signs indicating inferior alveolar nerve entrapment and pre-eruptive intra-coronal resorption in mandibular third molars

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I. Introduction

Inferior alveolar nerve (IAN) injury is one of the major complications of lower wisdom tooth extractions. The incidence of IAN injury and consequential temporary neurosensory disturbance ranges from 0.4% to 8.4%, whereas permanent damage usually remains under 1%. An extensive preoperative radiographic examination is inevitable for predicting the risks of third molar extraction. Panoramic radiography (PR) is usually the first-line tool recommended to assess impacted third molars and estimate the risk for IAN injury. Certain radiographic risk signs also called "classic specific high-risk signs" (*interruption of the superior cortical wall, narrowing and diversion of the canal, darkening of the root, narrowing or deflection of the root*) have been identified presuming a close spatial relationship between the tooth and the IAN. It was shown that a patient with one or more risk signs has a significantly higher risk for IAN injury, whereas in the absence of these signs the risk seems to be minimal. PR images alone are not sufficient enough to accurately predict the IAN-injury, therefore in high-risk cases cone-beam computertomograpy (CBCT) may be indicated to make the appropriate therapeutic decision. However, it is important to note that based on randomized controlled trials and systematic literature analysis the use of CBCT does not significantly reduce the occurrence of IAN-injuries.

In rare anatomic situations, the IAN perforates through the root of a lower third molar tooth or the roots completely surround the inferior alveolar canal (IAC). Pippi suggested the term *inferior alveolar nerve entrapment* (IANE) for these root conformations. Chopra et al. described these cases as Polo® mint mandibular third molars, as they resemble the shape of the Polo® mint candy. Although exact data on the occurrence of IANE are not currently available, it has been estimated to be 0.02-0.1% of lower mandibular third molar impactions.

Removal of an IANE tooth unequivocally increases the risk for IAN injury. Without correctly identifying the entrapment situation and without adequate tooth sectioning, the tooth mandatory ruptures the neurovascular bundle during removal. Some authors found that total removal of these third molars resulted in persistent anesthesia. On the other hand, treatment with coronectomy or careful sectioned tooth removal resulted in temporary hypoesthesia and paresthesia. Pippi et al. reported that no complications developed after careful sectioned removal of an IANE third molar case.

Radiographic signs indicating IANE third molars have been investigated previously. *Darkening* of the root, *interruption* of both cortical lines, *constriction* of the canal in the middle of the root,

and *diversion* of the canal have been suggested as correlates of IANE. Motamedi et al. stated that the *interruption* of both the superior and the inferior cortical lines is a reliable indicator for IANE. Other investigations found that the *upward* (cranial) *deviation* of the mandibular canal was highly predictive of IANE. Chopra et al., however, concluded that regardless of whether IANE cases are associated with multiple risk signs, it is impossible to reliably detect these cases based on two-dimensional radiographic imaging. In fact, no control group was analyzed in that case series.

The nerve entrapping root morphology can be clearly detected on cone beam computed tomography (CBCT) scans, as they allow for the elucidation of the exact relationship between the tooth and the mandibular canal. Although CBCT is more accurate for determining the position of the tooth, the number and morphology of the roots, bone coverage and density and the relationship between the roots and mandibular canal, it is still not recommended routinely.

Juxta-apical radiolucency is a radiographic sign appearing as a well-circumscribed radiolucent area at the apex and lateral to the root of mandibular third molars. Since the role of this sign in association with IAN-injuries was investigated about 15 years after the classic specific high-risk sings, we considered it to be important to present a review in the Hungarian literature, the summary of which can be read in the Discussion chapter.

Several alternative surgical techniques have been introduced that are aimed to reduce risk for IAN-injury. These are delayed tooth extraction following partial crown sectioning, pericoronal ostectomy, endoscope-assisted intraalveolar sectioned tooth extraction, coronectomy and orthodontic tooth extrusion. In the latter two procedures the condition of the crown may be an important limiting factor.

Pre-eruptive intra-coronal resorption is a well-circumscribed radiolucent lesion affecting unerupted or impacted teeth. It is predominantly localized in the coronal tissues and mostly affects the dentin adjacent to the enamel, however, according to Yüksel et al. the enamel and the root may also be affected. In most cases, PEIR is asymptomatic, and it is usually detected during routine radiological examinations. It is important to diagnose PEIR affecting mandibular third molars and thoroughly examine its characteristics (lesion size, localization, progression, involvement of the pulp) as PEIR also affects the applicability of surgical methods (coronectomy, orthodontic extrusion). The existing literature data is not sufficient enough to assess the prevalence and to describe the characteristics of PEIR in mandibular third molars.

II. Objectives

II.A. Identifying third molar cases with inferior alveolar nerve entrapment by analyzing panoramic radiographic signs

The aim of the present study was to identify any panoramic radiographic signs or their specific combinations that may reliably predict and locate IAN entrapment root conformations.

II.B. Pre-eruptive intra-coronal resorption in lower third molars

The aim of the study was to determine the prevalence of PEIR in impacted or unerupted mandibular third molars that do not communicate with the oral cavity, to describe its main characteristics, as well as the potential risk-increasing role of IAN-injury based on the analysis of panoramic radiographs.

III. Patients and Methods

III.A. Identifying third molar cases with inferior alveolar nerve entrapment by analyzing panoramic radiographic signs

In this case-control study, patients who were treated with at least one impacted lower third molar in our department (Dept. Oral and Maxillofacial Surgery, Medical School, University of Pécs, Pécs, Hungary) between May 2019 and December 2020 were included. Patients with diagnostically correct digital panoramic radiographs were enrolled when radiographs indicated an elevated risk for IAN injury according to the presence of one or more classic “high-risk” panoramic signs (i.e., Rood-Shehab’s risk signs) and when an overlap was observed between the IAC and the third molar. Panoramic radiographs were considered diagnostically correct if significant positional errors, and any disturbing artifact in the area of the lower third molars were absent. Further inclusion criteria were that patients also had CBCT images, which were indicated by the ad hoc clinical diagnostic team earlier, for the treatment decision (extraction/coronectomy/observation). Cases with incomplete root development, periradicular cysts or any other periapical radiolucent lesions other than juxta-apical radiolucency were excluded from the study.

Panoramic radiographs were taken with a PaX-400C unit (10.42 line pairs/mm, 73 kV, 10 mA) (Vatech, Gyeonggi-do, Korea), whereas CBCT examinations were performed with a GXDP-800 3D unit (KAVO- Gendex, Charlotte, USA) [90 kVp; 3.2-10 mA/6.1-8.5 s; FOV, 61 mm x 78 mm or 78 mm x 150 mm; focal spot, 0.5 mm; scan time, 10-20 s; slice thickness, 0.5 mm; voxel size, 0.2 mm]. Two experienced observers (K. J. and B. S.) analyzed the images independently during this study. Ambient light and the monitor used (high resolution, 19" in size) were constant. For panoramic radiographic image analysis, EasyDent (Vatech) software was employed. For CBCT analysis, the 'InvivoViewer' software (ver. 2.0.0., KAVO) was used. The IANE group consisted of cases in which CBCT unambiguously identified situations where the IAC was surrounded by third molar roots or the IAN was embedded in the root of the third molar tooth. For a proven "surrounded IAC" root conformation, roots had to be totally or subtotally closed around the neurovascular bundle. In the case of total closure, root tips were in contact with each other (or fused completely), whereas in subtotal closures, the gap was less than 1 mm between the root tips. In contrast, the control group was composed of cases where the IAC was not entrapped -independent of the possible interradicular course - between the third molar's roots according to the CBCT analysis.

The primary predictive variable was the presence or absence of one or more specific panoramic "high-risk" signs, indicating a close spatial relationship between the third molar tooth and the IAC. These "classic" markers were the interruption of the superior cortical line, interruption of both the superior and inferior cortical lines, diversion of the IAC (divided further to cranial "upward" and caudal "downward" diversion), narrowing of the IAC, darkening of the root, deflection of the root, mesiodistal narrowing of the root, bifid and dark root. Other predictive variables were gender, age, Pell-Gregory and Winter classifications, number of third molar's roots, extent of overlap of the root and the IAC and rotated third molar position. Overlap with the IAC was classified as follows: A) the root tip reached over the superior cortical line and was nearer to the superior line, B) the root tip was nearer to or in contact with the inferior cortical line (but did not reach over it) and C) one or more of the root tips reached over the inferior cortical line of the IAC. The rotated position of the third molar tooth was classified as "rotated significantly" or "not rotated significantly" according to the subjective impression and judgment of the two observers. To measure the correctness of the decisions in this special and highly subjective category, in 10 cases from the "rotated" and "not rotated" groups, the exact angle of rotation along the long axis was measured with the help of the built-in angle measurement tool of the CBCT program.

The outcome variable was the presence or absence of IAN entrapment in the roots of third molars.

III.B. Pre-eruptive intra-coronal resorption in lower third molars

A cross sectional retrospective study was conducted with the ethics license number 7920_PTE_2019 (Regional Research Ethics Committee PTE KK). The study material was collected from panoramic radiographs of patients presented at the Department of Dentistry Oral and Maxillofacial Surgery, University of Pécs between May 2019 and December 2022 for mandibular third molar extraction or orthodontic examination. Inclusion criteria was the presence of a mandibular third molar with PEIR lesion on the panoramic radiograph. Cases with inadequate quality of imaging (e.g.: artifact of positioning error), incomplete documentation, and communication between the PEIR lesion and the oral cavity were excluded. The eMedsolution medical administration software (T-Systems Hungary, Budapest, Hungary), paper-based patient documentations, PR images and, if available, CBCT scans were used for data collection.

The presence or absence of PEIR lesion in unerupted mandibular third molars was detected based on PR images. The digital images were taken with the PaX-400C device (with a maximum resolution of 10.42 line pairs/ mm, Vatech, Korea). The images were evaluated using EasyDent (Vatech) and VixWin Platinum (Gendex, Des Plaines, Illionis, USA) radiographic analysis software. The following integrated image manipulation tools were used for radiographic analysis: magnification, sharpness, contrast, inverse color display, brightness.

The PEIR lesions identified on PR images were classified according to the classification system published by Yüksel et al. in 2022. Additional data were collected regarding the relationship between the lesion and the pulp, the impaction status (Pell-Gregory classification) angulation (Winter classification), ectopic and rotated position of the affected teeth, as well as the presence of the panoramic high-risk signs. An ectopic position was considered when the tooth or the crown was located outside the dental arch based on its characteristic appearance on the PR image. Rotated position was considered when a characteristic image of the rotation around the long axis of the tooth was seen instead of the projection of the normal position on the PR image. The radiographic analysis was repeated one month after the first examination to evaluate the reliability of the examiners.

IV. Statistical analysis

IV.A. Identifying third molar cases with inferior alveolar nerve entrapment by analyzing panoramic radiographic signs

Data were collected and analyzed with SPSS 23.0 (SPSS, Chicago, IL, USA) and MedCalc (Ostend, Belgium) statistical software. The association of the variables with IAN entrapment status was tested by the Mann-Whitney 2-sample rank sum test for age and by the Fisher's exact test for gender and other predictive variables. The differences in the exact angles for the "rotated significantly" and "rotated insignificantly" decisions of the observers were estimated with the independent samples t-test. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (LR+) and accuracy (AC) were estimated for the radiographic signs indicating IAN entrapment. The predictive values were estimated according to Bayes theorem. The LR+ was calculated as sensitivity/(1-specificity), with the meaning of true positive rate per false positive rate. The accuracy and 95% confidence intervals (95% CI) of the radiographic signs were calculated using the following equation: sensitivity × prevalence + specificity × (1 – prevalence), meaning the overall probability that IAN entrapment was correctly diagnosed. A *p* value of <.05 was considered to be significant. Intra- and interobserver reliability were calculated by Cohen's kappa test, after both observers analyzed 30 panoramic radiographs three weeks later than the first round of analysis. A kappa value of <0.40 was considered to show poor agreement, a value of 0.40-0.59 fair agreement, a value of 0.60-0.74 good agreement, and a value of 0.75-1.00 excellent agreement.

IV.B. Pre-eruptive intra-coronal resorption in lower third molars

For statistical analysis data were processed using Microsoft Excel software (Office 365, Microsoft Corporation, Redmond, Washington, USA) and an online Mann-Whitney calculator was used. The results were considered significant if the value of $p< 0.05$.

Intra- and interexaminer reliability was determined using Cohen's Kappa test (ƙ<0,40 low agreement, ƙ:0.40-0.59 average agreement, ƙ:0.60-0.74 good agreement, ƙ:0.75-1.00 excellent agreement).

V. Results

V.A. Identifying third molar cases with inferior alveolar nerve entrapment by analyzing panoramic radiographic signs

In the examined 19-month period, 149 patients were judged to undergo CBCT after the panoramic radiograph because of the supposed increased IAN injury risk. In eight of these patients, IAN entrapment in third molar roots was proven by CBCT. In two patients, the IAN entrapment occurred bilaterally, resulting in 10 IANE cases. In the other 141 risk patients, resulting in 218 control cases, nerve entrapment was not observed.

The IANE group was significantly older by ~8.5 years than the control group (Mann-Whitney test, p=.021). There were more females both in the IANE (90.0%) and in the control (60.6%) groups than males; however, gender distributions were not different between groups (p=.094).

Regarding impaction patterns and tooth angulations, there were no significant differences between the study groups. The Pell-Gregory II/B position and vertical angulation were the most frequent types of impaction in both groups.

Considering the number of roots, third molars with two-roots were significantly less frequent in the IANE group (50.0%) than in the control group (80.7%) (p=.029). In contrast, third molars with four roots were significantly more frequent in the IANE group than in the control group (20.0% vs. 2.3%) (p=.009).

An unambiguous rotated third molar position was more frequently seen in the IANE group than in the control group (p<.001). The “rotated significantly” decision group had an average 46.4° rotation along the long axis, whereas in the “not rotated significantly” group, this was only 9.6°. This difference was statistically significant (t=4.39; p<.001; independent samples t-test), meaning that observers judged third molars as “rotated” in case of significantly higher twisting around the long axis.

Regarding the classic panoramic high-risk markers, interruption of the superior cortical line (p<.001), interruption of both cortical lines (p=.005), upward diversion of the IAC (p<.001) and darkening of the root (p=.015) signs were seen significantly more frequently in the IANE group than in the control group. In contrast, deflection of the root sign was more frequent in the control group (50.5% vs. 10.0%) (p=.019). Some specific combinations of radiographic markers were more frequently seen in the IANE group. These combinations were darkening of the root with interruption of the superior cortical line (p=.016), darkening together with interruption and

upward diversion of the canal (p<.001) and darkening with interruption and a rotated position of the third molar (p<.001). The sensitivities and specificities of the abovementioned signs or their examined combinations varied between 20.0% and 100.0% and between 61.9% and 100%, respectively. PPVs and NPVs of the signs considering the 4.4% prevalence were between 10.8% and 100.0% and 85.3% and 100.0%, respectively. The positive likelihood ratio, with the meaning of the true positive rate per false positive rate, was the highest in the case of upward diversion (LR+: 36.3) and interruption of both cortical lines (LR+: 43.6) signs and in the case when darkening, interruption and rotated position were in combination (LR+: 130.8). The accuracy of the radiographic markers was between 63.6% and 97.8%. Upward diversion of the IAC as a single sign (96.5%, [95% CI: 93.2%-98.5%]), or its combination with darkening and interruption (97.4%, [95% CI: 94.4%-99.0%]) and the combination of darkening with interruption and rotated third molar position (97.8%, [95% CI: 95.0%-99.3%]) had the highest accuracy in indicating an IAN entrapment situation correctly in this study.

The two observers had excellent (0.88 and 0.81) intraobserver and good (0.74) interobserver reliability based on kappa values in this study.

V.B. Pre-eruptive intra-coronal resorption in lower third molars

During the research period 6775 patiens presented at the Department of Dentistry Oral and Maxillofacial Surgery, University of Pécs for mandibular third molar removal (3632 patient) or orthodontic treatment planning (3143 patient). Based on the inclusion and exclusion criteria, 21 mandibular third molars with PEIR lesions of 20 patients were included in the study. Of these, 10 were unerupted developing teeth, and 11 were impacted teeth with fully developed roots.

The gender ratio in the studied population was 0.67 (8 men, 12 women).

The average age was 31 years (extreme values: 10-84 years, average deviation from the average: 21 years).

In one of the impacted teeth the resorption process was so advanced, that the impaction status could not be classified due to the small amount of remaining tooth. Of the remaining 10 impacted teeth 50% were PG I, 40% were PG II and 10% were PG III. Regarding the vertical component of the impaction 10% were PG A, 40% were PG B and 50% were PG C. Of the combinations 10% were PG I/B, 20-20% were PG I/C or PG II/C and 10-10% were PG II/A, PG II/B or PG III/C.

The distribution of the axis deviations according to Winter were as follows: 4.8% were horizontal (1/21), 52.4% were mesioangular (11/21), 38,1% were vertical (8/21) and 4.8% were distoangular (1/21).

47.6% of the teeth were ectopic (10/21) and 42.9% were rotated (9/21), in one case the rotated status could not be correctly classified due to severe resorption.

Regarding the classic specific high-risk signs among the impacted teeth in 66.3% darkening of the root (7/11), in 54.5% diversion of the mandibular canal (6/11), in 36.6-36.6% interruption of the cortical line (4/11) or deflection of the root (4/11), in 27.3% narrowing of the mandibular canal were observed. Isolated root darkening was observed in 42.9% (3/7) of impacted teeth, while it occurred in combination with other risk signs in 57.1% (4/7), predicting an increased risk for IAN-injury.

The distribution of PEIR lesions based on the classification of Yüksel was as follows: 23.8% of the examined teeth were grade 2 (5/21), 9.5% were grade 3 (2/21), 4.8% were grade 4 (1/21), 23.8% were grade 5 (5/21), 9.5% were grade 6 (2/21), 4.8-4.8% were grade 7 (1/21), grade 11 (1/21), and grade 12 (1/21), 14.3% were grade 13 (3/21). With the exception of one grade 13 case the grade 11 or above PEIR lesions caused pulp involvement, which was detectable on PR images.

In case of deep lesions and root involvement multiplex root darkening was seen in 66.7% (4/6) of cases, while regarding all PEIR cases it was only observed in 19% (4/21).

Patients with more extensive lesions (≥7) were significantly older than those with smaller lesions (<7) (50.3± 18.3 vs. 23.7± 15.2 years; p=0.0128, Mann-Whitney-test).

Intraexaminer (ƙ=0.78; ƙ=0.81), and interexaminer (ƙ=0.76) reliability were proved to be excellent.

VI. Discussion

VI.A. Identifying third molar cases with inferior alveolar nerve entrapment by analyzing panoramic radiographic signs

This retrospective case-control study confirmed that IANE root configuration can be correctly predicted with the help of analyzing relevant panoramic radiographic signs.

Several investigations found previously that three of the classic radiographic signs, namely, darkening of the root, interruption of the superior cortical line and diversion of the canal may predict a close spatial relationship between the root and the mandibular canal. The close anatomic relationship increases the risk for IAN injury. In the current research, the IANE situation was also significantly associated with these signs. However, the PPV and accuracy of root darkening and interruption of the superior cortical line were found to be low (PPVs: 10.8% and 20.1%; AUCs: 63.6% and 85.1%) meaning that in most cases showing these signs, IANE was eventually not observed. NPVs were found to be high for all these radiographic signs, meaning that in the absence of these signs, the presence of IANE is unlikely (85.3%, 96.4%, 97.7%).

During the investigation, it became clear that the "diversion of the canal" sign had to be further classified as "downward" (caudal) and "upward" (cranial) bending of the IAC. We found that upward diversion was significantly associated with IANE (LR+: 36.3; AUC: 96.5%), whereas downward diversion remained insignificant. This is in correlation with the findings of Pippi and Chopra et al., who suggested the upward deviation of the mandibular canal to be highly predictive for IANE. In a cross-sectional radiographic study, Tassoker found that the diversion of the mandibular canal strongly correlates with the absence of cortication of the IAC; furthermore, in the case of an interradicular canal course in 100% of cases, IAC fenestration was observed. Unfortunately, the aforementioned study did not specify the direction of the diversion.

Interruption of the cortical borders has been attributed to the absence of cortical structure between the canal and the root. Motamedi found interruption of both the upper and the lower cortical borders in correlation with IANE. In our study the interruption of both cortical lines was a rare finding and occurred in only three cases (1.3%). Among these, 2 cases were proved in the IANE group. In the third case, although complete entrapment was not found, an interradicular course of the nerve and a significant groove on the lingual root were observed.

Based on this finding, the interruption of both cortical lines seems important and predictive of interradicular and probably surrounded IAN root conformation (LR+:43.6; AUC: 96.0%). In addition to the significance of the single occurrence of upward diversion or interruption of both cortical lines, some combinations of the investigated radiographic markers were found to be accurate in predicting IANE situations. Based on our results, the simultaneous presence of root darkening, interruption of the superior cortical line and upward diversion of the canal or the rotated position of the third molar along its long axis was the most predictive factor for IANE, with the highest AC values (97.4% and 97.8%).

Analyzing the previously published IANE cases in the literature, in correspondence with our results, three out of seven reported cases showed the combination of root darkening, interruption of the superior cortical line and upward diversion of the canal. Rotation of the third molar was also found in three cases. In addition, Chopra et al. reported a series of 22 cases, where 86% of the IANE third molar cases showed two or more "classic specific risk signs" simultaneously on panoramic radiographs; however, none of the signs were present in all of the cases.

According to the recommendation of the European Academy of Dentomaxillofacial Radiology, CBCT imaging of the mandibular third molar should not be routinely applied. When the abovementioned panoramic risk signs are present, especially in combination, CBCT evaluation is highly recommended before total tooth removal. CBCT imaging may confirm and show the IANE situation in detail and therefore, may also change treatment decisions or determine the exact steps of surgical removal.

Retention of IANE molars with conservative treatment, improved oral hygiene and monitoring should be targeted whenever possible according to Chopra et al. In a recent systematic review Ghaeminia et al. concluded that there is insufficient evidence regarding whether asymptomatic, disease-free impacted third molars should be retained or removed. In these cases, the risks of surgical intervention must be weighed against possible future complications of tooth retention in decision making. However, there is no approved management technique for treating IANE third molars, and earlier studies suggested coronectomy or careful sectioned removal.

Coronectomy effectively reduces the risk for IAN. The major drawback of this technique, however, may be postoperative root migration. After coronectomy, the migrating IANE root residuals can dislocate the neurovascular bundle, which may lead to later neurological complications. If roots are mobilizing during coronectomy, they have to be removed after careful separation.

Another alternative therapy to reduce the risk for IAN injury is orthodontic tooth extrusion, which aims to dislocate root tips from the neurovascular bundle prior to surgery. In the case of IANE third molars, the neurovascular bundle itself migrates with the tooth, resulting in a reduced or limited advantage of this technique. However, a more superficially moved impacted tooth might be more precisely and easily sectioned and removed.

If dental or periodontal pathology indicates complete removal of the IANE third molar, careful sectioning is mandatory to prevent IAN injury. Sectioning must be extremely cautious not to harm the neurovascular bundle and the usage of depth-controlled preparation, non-rotating (piezoelectric) preparation tools and careful elevator usage should be considered.

In our study sample, out of 10 IANE cases, five teeth were retained and regularly observed, and three coronectomies and two sectioned removals were performed. Permanent neurosensory disturbance was not observed in the invasively treated cases.

Due to its rare occurrence, however, only a low number of IANE cases could be evaluated. It should also be mentioned that the identification of radiographic signs is slightly subjective and highly dependent on the investigator's experience.

VI.B. Pre-eruptive intra-coronal resorption in lower third molars

In the review of Al-Batayneh and Al-Tawashi, where 12 studies were summarized, PEIR was found in 835 of the total of 30017 patients (2.78% patient prevalence), while in 896 of the total of 91751 teeth (0.98% prevalence of teeth). However, according to Demirtas et al., with the use of CBCT significantly more PEIR cases may be revealed compared to PR images. In our retrospective analysis PEIR affecting mandibular third molars was detected in 0.3% of patients (21/6775).

Based on literature data, ectopic tooth position may be observed in 13-28% of PEIR cases. In contrast, Demirtas et al. found ectopic position in nearly 50% of cases. In our study, we found ectopic position in 47,6% (10/21) and rotated position in 42,9% (9/21) of PEIR cases.

According to literature data the lower and the upper first molars, the lower second premolar and second molars are most affected by PEIR. In the study of Umansky et al. 23% of PEIR lesions (3/13) occurred in mandibular third molars. Interestingly, a recent systematic review on the therapy of PEIR lesions mentioned only one case report involving a mandibular third molar.

Ideally, there is definite indications and patient motivation for the removal of third molars, while the risk for major complications is low. In case of PEIR lesions, concerns arise. It is very difficult or almost impossible to differentiate between a regular caries and PEIR, however, deep

bony impaction without any communication with the oral cavity may support the diagnosis of PEIR. On the other hand, it is questionable that which treatment strategy would be optimal in case of “high risk” mandibular third molars. In all cases presented in our case report the IAN was exposed after tooth extraction. The fenestration of the mandibular canal and subsequent IAN exposure increases the risk for IAN-injury. In addition, direct and indirect heat demage and the postoperative inflammatory process may affect the neurovascular bundle. For such high-risk cases, when pathologic indications are absent, observation or coronectomy is a good alternative. However, coronectomy is not recommended in case of coronal defects. Surgical tooth removal can bear the risk of IAN injury, while observation is unpredictable in the long term. In our study 19% of the mandibular molars (4/21) were at risk for IAN-injury based on the radiographic risk signs. However, considering only those teeth with advanced lesion (≥7) then multiplex root darkening, as one of the strongest predictor for IAN-injury, was present in 66.7% of cases (4/6).

According to Spierer and Fuks, the decision to “treat or not” depends on the progression of the lesion and its proximity to the pulp. Regarding the course of the disease, progressive and non-progressive forms of PEIR can be differentiated. In the case of small lesions, radiological follow-up with a 6-12-month interval was an alternative suggested recently. However, it should also be considered that third molar wound healing can deteriorate with age.

Additionally, when PEIR is uncontrolled and mucosal rupture or eruption occurs, bacterial invasion undoubtedly triggers caries. Untreated caries and subsequent pulpal necrosis can lead to periapical chronic inflammation and lesions, and periapical lesions involving the IAC may also cause neurosensory disturbances. Surgical removal is the only alternative treatment for these third molars.

In several small-or moderate-size PEIR lesions, a normal dentine layer was found between the lesion and pulp, without secondary dentin deposition, and with healthy uninflamed pulp tissue. In such cases, restorations employing gentle curettage of the lesion using hand instruments, filling with glass ionomer cement, or amalgam or zinc-oxide eugenol restorations have been successful. Pulp exposure without signs of inflammation was successfully treated by direct pulp capping with calcium hydroxide, mineral trioxide aggregate or Biodentine prior to the abovementioned restorations. From this point of view, coronectomy may be successful in cases of PEIR defects without pulp involvement. To determine the exact extension and pulpal border of the PEIR defect, thorough analysis and use of CBCT are unavoidable. Further studies are required to investigate the postoperative course and safety of coronectomy in cases of third

molars with small and moderate sized PEIR. In our study small and moderate sized PEIR lesions were found in 71.4% of cases.

Orthodontic-assisted tooth extraction could also be considered to reduce the risk of IAN injury. The authors proposed two theoretical concerns regarding the use of this method in PEIR cases. On one hand, the condition of the crown and adhesion surface may determine or limit the adhesion quality. On the other hand, traction elements work through mucosal fenestration, allowing for microorganism penetration during the extraction period, which may be accompanied by caries transformation and pulpal necrosis.

VI.C. Juxta-apical radiolucency of mandibular third molars

A radiographic sign recently associated with IAN-injury is the juxta-apical area, also known as juxta-apical radiolucency. JAR is a well-defined radiolucent area appearing at the apical and lateral surfaces of mandibular third molars. It is common, occurs in approximately 33% of patients, and mostly affects young women. The radiolucency can usually be distinguished from the mandibular canal, and it is most likely caused by the superimposition of highly separated bone trabeculae. Although some authors have described an increased tendency of IAN-injury in the presence of JAR, the study specifically investigating this relationship refuted the role of JAR as an independent risk factor in the occurrence of IAN-injury. It may rise important diagnostic problems, when needed to be differentiated from other radiolucent lesions in the mandible. Furthermore, due to its common overlap with the mandibular canal, it may complicate the analysis of the classic specific risk signs or even indicate modification of the surgical technique or even the use of three-dimensional imaging.

VII. Conclusion of novel results

Based on our retrospective case-control study entitled *Identifying third molar cases with inferior alveolar nerve entrapment by analyzing panoramic radiographic signs* the following conclusions can be made:

- The IANE conformation can be predicted by analyzing relevant radiographic signs on PR images
- The combination of darkening of the root, interruption of the upper cortical line of the mandibular canal, upward diversion of the mandibular canal or the rotated position of the mandibular third molar is the most reliable predictive factor for IANE
- Interruption of both cortical lines of the mandibular canal is a significant risk sign of an interradicular and possibly surrounded neurovascular bundle

Based on our cross-sectional study entitled *Pre-eruptive intra-coronal resorption in lower third molars* the following conclusions can be made:

- PEIR also affects mandibular third molars (0.3%)
- PEIR is often observed in ectopic (47.6%) or rotated (42.9%) mandibular third molars
- In case of advanced PEIR lesion in mandibular third molars, radiographic signs indicating risk for IAN-injury can often be observed (66.7%)
- The presence and character of the PEIR lesion may modify and determine the follow-up schedule of cases, as well as it may influence therapeutic decisions, forcing the practitioner to choose between restorative solutions, coronectomy and total tooth extraction

Publications

Publications related to the Ph.D. thesis:

Janovics K, Soós B, Tóth Á, Szalma J. Is it possible to filter third molar cases with panoramic radiography in which roots surround the inferior alveolar canal? A comparison using cone-beam computed tomography. *J Craniomaxillofac Surg*. **2021**; 49: 971-979. doi: 10.1016/j.jcms.2021.05.003.

*Scimago: **D1**; IF: **3,192*** *Independent citation: **4***

Janovics K., Soós B., Lempel E., Bán Á, Szalma J. Az alsó bölcsességfogak juxta-apikális radiolucenciája: Irodalmi összefoglaló. *Fogorv Szle.* **2021**; 114: 106-112. https://doi.org/10.33891/FSZ.114.3.106-112

Janovics K., Soós B., Gurdán Zs, Pacheco AE, Lempel E., Bán Á, Szalma J. A pre-eruptív intrakoronális lézió előfordulása és jelentősége bölcsességfogak esetében. *Fogorv Szle*. **2023**; – accepted for publication

Szalma J, **Janovics K**, Pacheco A, Kaszás B, Lempel E. Pre-eruptive intracoronal resorption in "high-risk" impacted third molars: A report of four cases. *J Craniomaxillofac Surg*. **2022**; 50(10): 798-805. doi: 10.1016/j.jcms.2021.05.003

*Scimago: **D1**; IF: **3,192***

Publications independent from Ph.D. thesis:

Soós B, **Janovics K**, Tóth Á, Di Nardo MD, Szalma J. Association Between Third Molar Impaction Status and Angle or Condylar Fractures of the Mandible: A Retrospective Analysis. *J Oral Maxillofac Surg. **2020***; 78(7): 1162.e1-1162.e8. doi: 10.1016/j.joms.2020.02.005.

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*Scimago: **Q4**; IF: **0,54*** *Independent citation: **1***

Cumulative impact factor of thesis related publications: 6,384
Cumulative impact factor of all publications: 8,819