Original Article

JOMP
Journal of Oral Medicine and Pain

pISSN 2288-9272 eISSN 2383-8493
J Oral Med Pain 2016;41(3):118-125
http://dx.doi.org/10.14476/jomp.2016.41.3.118

Clinical Predictors of Permanent Neuropathy in Patients with Peripheral Painful Traumatic Trigeminal Neuropathy

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Received August 18, 2016
Revised September 8, 2016
Accepted September 8, 2016

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This study was supported by research fund from Chosun University, 2014.

Purpose: The aims of this study were to evaluate the clinical characteristics of patients with altered sensation and/or pain, and to determine outcome predictors affecting persistent neuropathy.

Methods: Patients who complained an altered sensation or pain following trigeminal nerve trauma were involved in this study. To determine outcome predictors affecting persistent neuropathy, the patients were divided into two groups; transient vs. persistent, and the clinical phenotypes are compared between groups. Data were analyzed with t-tests, chi-square, and multiple regression analyses with 95% confidence interval and $p<0.05$ significance level.

Results: A total of 111 patients were included: 23 with transient and 88 persistent groups. The panoramic result and pin-prick test score were statistically different between the groups. Radiating symptoms after blunt and pinprick stimuli were also significantly different between groups. The results revealed that the presence of a neurologic lesion in the panoramic view result, reduced sensation in the pinprick test, and radiation in the pinprick test could affect the persistent group.

Conclusions: The presence of a neurologic lesion in panoramic view result and reduced sensation and radiating symptoms in the pin prick test would be defining features of one of the main clinical features of persistent neuropathy. These features could serve as outcome predictors diagnosing the permanent nerve injury in trigeminal nerve.

Key Words: Iatrogenic; Nerve injuries; Outcome predictor; Trigeminal nerve; Wounds and injuries

INTRODUCTION

Nerve damage from variety of factors can cause chronic neuropathic pain. Iatrogenic nerve damage, especially, can result in medico-legal issues. In dentistry, the treatment itself is the surgical approach, and can cause harm to the peripheral nerve, which in the orofacial area is a portion of the trigeminal nerve. Dental treatments with reports of nerve injury include the Caldwell-Luc intervention, orthognathic mandibular advancement surgery, extrusion of root canal filling material, administration of local anesthetic, and implant surgery, with third molar extraction as the most frequent cause.[1,2] All these changes can be transient or persistent depending on the degree of the nerve insult.[3]

Nerve damage can affect a single nerve or several nerves, and result in sensory, motor, and/or autonomic deficits in the affected region.[2] Damage to sensory nerves can result in anesthesia, paraesthesia, pain, or a combination of the three. The resulting pain could also create significant functional problems.[4] Patients with trigeminal nerve trauma often complain that the sensory disturbance and/or pain interfere with daily function, decreasing quality of life and potentially leading to significant psychosocial problems.[5] The significant disability associated with these nerve injuries may also result in increasing numbers of medico-legal claims.[4)]

According to the report of the Korea Consumer Agency, out of 302 cases seeking legal redress for dental treatment, 101 cases (33.4%) were compensated and reimbursed. The number of cases of sensory alteration was 34, 11.3% of all medico-legal claims. The average amount of indemnity was 9,670,000 Korean Won (KRW) in cases of lingual nerve injury (LNI), and 6,230,000 KRW in those of inferior alveolar nerve injury (IANI). Especially, in cases of dental implant placement, the indemnity was judged about 31,360,000 KRW.

Because of these high indemnities, and for the patients' and clinicians' own well-being, clinicians should make particularly strong efforts to prevent iatrogenic nerve damage. However, if patients complain about altered sensation and/or pain after dental procedures, these patients should be reassessed for their conditions, medically managed for them when needed, and referred to orofacial pain or oromaxillofacial surgical specialists for proper treatment. In addition, orofacial pain or oromaxillofacial surgical specialists should diagnose their conditions properly, and assess risk factors for chronic neuropathy, to provide them with realistic outcome expectations.

Unfortunately, neuropathic pain due to trigeminal injury has been poorly defined. There are no standards or physical examinations to diagnose these conditions. In a recent article, diagnostic criteria for "peripheral painful traumatic trigeminal neuropathy (PPTTN)" were proposed.[6)] In that study, clinical phenotypes were compared between PPTTN patients and classical trigeminal neuralgia, and the study concluded that PPTTN criteria could be clinically useful. However, the clinical symptoms and pathophysiology of these two disorders are completely different. The main target population would be patients with altered sensation and/or pain, which is the typical symptom of PPTTN.

Consequently, the aims of this study were to evaluate the clinical characteristics of patients with with altered sensation and/or pain using PPTTN criteria, and to determine outcome predictors affecting persistent neuropathy.

MATERIALS AND METHODS

1. Subjects

This was a retrospective study of patients who complained of altered sensation or pain following trigeminal nerve trauma, from 2010 to 2013, who were visiting the Department of Oral Medicine, Chosun University Dental Hospital (Gwangju, Korea).

This study was not confined to patients with iatrogenic nerve damage. Trigeminal neuropathic symptoms after fractures or traffic accidents could also be subjects of insurance claims, so these cases were also included.

Patients with trigeminal neuropathy caused by systemic disease or local inflammation were excluded in this study. In addition, studied population was confined to the distribution of the trigeminal nerve third branch, i.e., symptoms affected to the first and second branches of the trigeminal nerve were excluded.

This study was approved by the Institutional Review Board of Chosun University Dental Hospital, 2013 (CDMD IRB-0903-27).

2. Methods

The patient histories and clinical examinations were documented according to routine procedures for sensory alteration after trauma in the Department of Oral Medicine, Chosun University Dental Hospital. Demographic data collected from each patient included age of onset and gender. From consecutive records, patients for whom the symptoms resolved in less than 3 months were designated the transient group. The persistent group was comprised of patients whose symptoms continued for more than 3 months after trauma, according to patient history or consecutive records. From the included population's medical records, variables were collected for comparison with those of the previous study.[6)]

1) Variables from patient history

Pain intensity was measured using a visual analogue scale (VAS), where 0 was no pain and 10 was worst pain imaginable. To match variables with the previous study,[6)] the quality of the pain was adjusted by one doctor (J.W.R.) after reviewing the medical records, who chose one or more of the following descriptive terms: electrical, stabbing, throbbing, pressure, burning, or any combination of the five terms. This was the same for the temporal patterns, adjusted according to attack frequency and duration parameters: episodic, daily, and continuous. Patients were asked to report the pain duration representing that of a typical attack. The presence of autonomic signs such as tearing, redness, or swelling was also recorded. Patients were asked about their quality of sleep after the symptoms started. A trauma history was collected verbally and from relevant documentation (e.g., third molar extraction, dental implant, traffic accident, fracture of jaws, etc.).

2) Variables from clinical examination

The clinical examination included mechanosensory testing, and radiographic examination, to assess the subjective symptoms of patients. Mechanosensory testing of the affected and contralateral areas included the use of pinprick stimuli (with a dental explorer) and blunt stimuli (with cotton swabs). Except for patients with lingual nerve damage only (6 cases), all mechanosensory tests were given to the extraoral affected area. During the test, patients were asked to rate of response to each stimulus based on a scale of 0 to 100, such that 0 meant a complete sensory deficit to the given stimulus, while 100 meant the same intensity of feeling as that of the contralateral area. When patients reported sensitivity over 100 (hypersensitivity), they were asked to rate the feeling numerically (>100). These tests were complemented by examining the radiating sensation caused by each stimulus. For statistical analysis, the scores of each stimulus were categorized into 4 degrees: very low (0-39), low (40-79), normal (80-119), and high (≥120). The mechanosensory tests were repeated three times. Based on these tests, affected areas were diagnosed as to “sensory signature” to match the diagnoses of the previous study.[6] In addition, patients who agreed to further evaluation procedures for defining their symptoms underwent quantitative sensory testing (QST) using transcutaneous electrical stimuli delivered by the Neurometer Nervscan NS3000 device (Neurotron, Baltimore, MD, USA). The Neurometer QST procedures were matched with another previous study that evaluated neurosensory alteration in orthognathicsurgeries.[7] Stimuli were delivered at 250 Hz to assess the sensory threshold associated with A-δ fiber stimulation, and at 2,000 Hz and 5 Hz for A-β and C fiber evoked sensory thresholds, respectively. Subjects were instructed to release a control button upon the first sensation. Both operator and patients were blinded to the stimulus intensity provided. The scores obtained with each stimulus were converted ratios, of the affected area to the contralateral area.[6]

All patients underwent panoramic radiographic examination to evaluate the nerve injury. Additional cone-beam computed tomography (CBCT) imaging was taken to patients who agreed to further evaluation in order to locate and grossly assess the extent of nerve damage.

3) Determination of outcome predictors affecting permanent neuropathy

To find out the statistical differences between the transient and persistent groups, statistical analysis was performed via Pearson’s chi-square test (χ^2). Differences between continuous variables (onset age and pain intensity) were analyzed with Student’s t-test.

To explore possible contributing factors affecting the permanence of nerve injury, the above variables with significant differences were analyzed with multiple regression analysis.

3. Statistical Analyses

Data were analyzed with PASW Statistics 18.0 for Windows (IBM Co., Armonk, NY, USA).

Statistical significance was defined as $p<0.05$, with a 95% confidence interval.

RESULTS

In total, 111 patients were collected for the study, of whom 5.4% presented with LNI (6 patients) and 94.6% with IANI (105 patients). The transient group was comprised of 23 patients and the persistent group was comprised of 88 patients.

1. Comparison of Patient Profiles between the Transient and Persistent Groups

The demographic features of each group are summarized in Table 1. There were no differences in onset age or gender

Table 1. Demographic findings (age, gender ratio) in transient and persistent group

	Transient (n=23)	Persistent (n=88)	Total (n=111)
Onset age (y)	40.30±16.25	46.51±15.27	45.23±15.61
Gender (M:F)	8:15	35:53	43:68

M, male; F, female.
Values are presented as mean±standard deviation or number only.

Table 2. Distributions of initiating events affecting altered sensation or pain

Cause	No. (%) of cases
Anesthesia	3 (2.7)
Mass	5 (4.5)
Endo	9 (8.1)
Extraction	25 (22.5)
Fracture	18 (16.2)
Orthognathic	8 (7.2)
I/d	1 (0.9)
Implant	31 (27.9)
OPD/perio	5 (4.5)
Wound	6 (5.4)

Endo, endodontic treatment; I/d, Incision and drainage; OPD/perio, operative dental treatment and periodontic treatment.

ratio between groups.

In evaluation of the location, the left side was affected in 50 cases (45.1%), and the right side was in 48 cases (43.2%). Both sides (mentum area) were affected in 13 cases (11.7%).

The distributions of initiating events causing altered sensation or pain are summarized in Table 2, while the differences between patient profiles in the transient and persistent groups are described in Table 3. Patients in the transient group mostly reported the quality of pain to be pressure (73.9%), while the persistent group mostly reported burning pain (60.2%). Within groups, there were no significant differences in quality descriptors (χ^2, p>0.05).

Pain intensity showed no differences in VAS scores between groups. The average (mean±standard deviation) scores of pain intensity were 5.09±1.98, and 5.48±1.97 in the transient and persistent groups, respectively.

In evaluation of temporal patterns, most patients reported continuous (87.0% and 90.9% in the transient and persistent groups, respectively) pain, with no significant differences between groups.

For 35 patients, quality of sleep was reported as bad

Table 3. Differences between patient profiles in transient and persistent group

Parameter		Transient (n=23)	Persistent (n=88)	p-value[a]
Gender (M:F)		8:15	35:53	0.662
Onset age (y)		40.30±16.25	46.51±15.27	0.09[b]
Intensity (VAS)		5.09±1.98	5.48±1.97	0.399[b]
Temoral pattern				
Daily		3 (13.0)	8 (9.1)	0.695
Continuous		20 (87.0)	80 (90.9)	
Autonomic				
No		22 (95.7)	85 (96.6)	0.999
Yes		1 (4.3)	3 (3.4)	
Quality of pain				
Electric	No	15 (65.2)	47 (53.4)	0.310
	Yes	8 (34.8)	41 (46.6)	
Stabbing	No	15 (65.2)	58 (65.9)	0.950
	Yes	8 (34.8)	30 (34.1)	
Throbbing	No	23 (100.0)	84 (95.5)	0.579
	Yes	0	4 (4.5)	
Pressure	No	6 (26.1)	36 (40.9)	0.192
	Yes	17 (73.9)	52 (59.1)	
Burning	No	12 (52.2)	35 (39.8)	0.284
	Yes	11 (47.8)	53 (60.2)	
Sleep quality				
No change		17 (73.9)	59 (67.0)	0.439
Bad		6 (26.1)	29 (33.0)	
Panorama				
Yes		9 (39.1)	56 (63.6)	0.034*
No		14 (60.9)	32 (36.4)	

M, male; F, female; VAS, visual analogue scale.
Values are presented as number only, mean±standard deviation, or number (%).
[a]Pearson's chi-square test (except onset age and pain intensity).
[b]Student's t-test.
*p<0.05.

because of the trauma. This variable was not statistically different between the groups.

In the radiographic imaging tests, there was a significant difference (p<0.05) in the panoramic view test. All patients underwent panoramic radiographs, and 59 patients (53.2%) also underwent CBCT imaging of the area. There were 14 positive signs of nerve damage using CBCT out of 46 cases (30.4%), while in panoramic view there were no sign.

In the results of mechanosensory testing, most patients suffered from reduced sensation compared to the contralateral area (Table 4). With blunt mechanical stimulus from cotton swabs, 73.9% of the transient and 61.4% of the persistent group reported reduced sensation. With pin stimulus, 69.5% of the transient and 59.1% of the persistent group reported reduced sensation. Between groups, there was a statistically significant difference in the result of the pinprick test ($p<0.05$). Radiating symptoms after blunt and pinprick stimuli were also significantly different between groups.

Eleven patients in the transient and 67 patients in the persistent group underwent the QST procedures with the Neurometer. The ratios of the scores (affected area: contralateral area) in A-β, A-δ, and C fibers were all significantly higher than expected, but between the groups, there were no differences.

Diagnoses of sensory signatures are described in Table 5. In the transient group, hypoesthesia and hypoalgesia were the main features of the sensory signature. In the persistent group, hypoesthesia, hypoalgesia, and allodynia were the main features. Between groups, there was a statistically significant difference in the allodynia signature ($p<0.01$).

Table 4. Differences between results of mechanosensory testing in transient and persistent group

Physical exam		Transient (n=23)	Persistent (n=88)	p-value[a]
Blunt stimulus	Very low	11 (47.8)	19 (21.6)	0.074
	Low	6 (26.1)	35 (39.8)	
	Normal	2 (8.7)	10 (11.4)	
	High	4 (17.4)	24 (27.3)	
Radiating after blunt stimulus	No	17 (73.9)	29 (33.0)	0.000***
	Yes	6 (26.1)	59 (67.1)	
Pin stimulus	Very low	13 (56.5)	24 (27.3)	0.012*
	Low	3 (13.0)	28 (31.8)	
	Normal	0	13 (14.8)	
	High	7 (30.4)	23 (26.1)	
Radiating after pin stimulus	No	19 (82.6)	38 (43.2)	0.001**
	Yes	4 (17.4)	50 (56.8)	

Values are presented number (%).
The sum of the percentages may not equal 100% because of rounding.
[a]Pearson's chi-square test.
*p<0.05, **p<0.01, ***p<0.001.

2. Outcome Predictors Affecting Persistent Neuropathic Symptoms

Based on the chi-square and t-tests, the variables with significant differences between groups were identified: panoramic view result, reduced sensation, and radiation in the pinprick test, radiation in the blunt stimulus test, and allodynia. Multiple regression analysis was then performed on these variables (Table 6). The results revealed that the presence of a neurologic lesion in the panoramic view result, reduced sensation in the pinprick test, and radiation in the pinprick test could affect the persistent group, with Nagelkerke's R^2 calculated to be 0.607.

DISCUSSION

Recently, traumatic trigeminal neuropathy has been a significant research interest for dentistry.[5,8] It is a major, largely unrecognized clinical problem, which is distressing for

Table 5. Diagnoses of sensory signatures

Sensory signature		Transient (n=23)	Persistent (n=88)	p-value[a]
Hypoalgesia	No	7 (30.4)	30 (34.1)	0.741
	Yes	16 (69.6)	58 (65.9)	
Hyperalgesia	No	16 (69.6)	64 (72.7)	0.763
	Yes	7 (30.4)	24 (27.3)	
Hypoesthesia	No	4 (17.4)	24 (27.3)	0.331
	Yes	19 (82.6)	64 (72.7)	
Hyperesthesia	No	19 (82.6)	64 (72.7)	0.331
	Yes	4 (17.4)	24 (27.3)	
Allodynia	No	16 (69.6)	27 (30.7)	0.001**
	Yes	7 (30.4)	61 (69.3)	

Values are presented as number (%).
[a]Pearson's chi-square test.
**p<0.01.

Table 6. Outcome predictors affecting persistent neuropathy

Variable	β	Wald	Nagelkerke's R^2	Exp(B)
Panoramic view result	1.449	7.751**	0.607	4.258
Normal or exaggerated sensation in the pinprick test	−0.536	1.405		0.585
Reduced sensation in the pinprick test	−2.018	5.778*		0.133
Radiating after blunt stimulus	1.749	1.273		5.751
Radiating after pin stimulus	1.917	5.606*		6.798
Allodynia	−0.232	0.022		0.793

*p<0.05, **p<0.01 (by the Wald test).

and reduces the quality of life of patients.[9,10]

In this study, enrolled patients were grouped according to duration of symptoms, with the critical time set at 3 months. Defining the time at which permanent nerve injury is diagnosed might be performed differently by different authors. In most previous articles, injuries were regarded as permanent if the patient had symptoms for more than 6 months, because paresthesia was found to be temporary, and tended to subside within the first 6 months.[5,11-13] Based on these studies, clinicians have a tendency to instruct patients who show signs of nerve damage to wait at least six months. However, full recovery of nerve function is less likely when the patient is seen a long time after a severe injury.[5] Furthermore, proposing the PPTTN criteria defined as PPTTN as having continued symptoms for 3 months. This was in line with a recent review article that posited that after 3 months, permanent central and peripheral changes occur within the nervous system subsequent to injury that are unlikely to respond to surgical intervention.[10,14] Furthermore, it is important to differentiate neuropathic from non-neuropathic causes for the diagnosis and treatment of the conditions. A key feature of neuropathic pain is the combination of sensory loss with paradoxical hypersensitivity. Damage to the afferent transmission system causes partial or complete loss of input to the nervous system, leading to negative sensory phenomena, such as loss of touch or temperature or pressure sensations.[13] In contrast, inflammatory pain heightens pain sensitivity in response to tissue injury and inflammation, and it is also associated with hypersensitivity to normal sensory inputs.[10] Accordingly, symptoms that occurred for less than 3 months could originate from either inflammatory or neuropathic conditions. Therefore, defining the time between transient and persistent neuropathy as 3 months in this study seemed most appropriate.

In this study, most patients (84 out of 111, 75.7%) had neuropathic pain, while only 17 patients had lowered or completely numb sensation without pain. It is known that approximately 35% of chronic pain patients suffer from neuropathic pain.[5] Following the injury to trigeminal nerve branches, chronic pain develops in about 3%-5% of patients.[6,15] These symptoms coupled with neuropathic pain could be especially troublesome to patients, and result in a severe reduction of their overall quality of life.

The distributions of initiating events affecting altered sensation or pain are summarized in Table 2. Injury to the trigeminal nerve may occur from a variety of different dental treatments, including third molar extraction,[16] implant placement,[17,18] dental local anesthetic injection,[19] endodontic treatment,[20] and orthognathic surgery.[21] Non-iatrogenic causes such as skull fracture could also result in considerable nerve injury. In this study, implant placement caused the highest incidence of trigeminal nerve injuries (27.9%). In contrast, previous studies state that third molar extraction caused the highest incidence of iatrogenic trigeminal nerve injuries,[9,22] which was the second most common cause in this study (22.5%). Local anesthetic-related injury was only 2.7% of the incidence in this study. The difference could be explained by the fact that neuropathy related to third molar extraction or local anesthetic injection is usually temporary,[23] and thus patients do not seek secondary or tertiary referrals. Notably, some patients develop chronic neuropathic pain following negligible nerve trauma such as suturing of wounds, operative dental treatment, and periodontic treatment.

In the comparison of patient profiles, the presence of a neurologic lesion in the panoramic view result, reduced sensation and radiation in the pinprick test, radiating sensation with the blunt stimulus, and allodynia showed differences between the transient and persistent groups (Table 6). According to the result of the multiple regression analysis, the presence of a neurologic lesion in panoramic view result and reduced sensation and radiating symptoms in the pinprick test would be defining features of one of the main clinical features of persistent neuropathy. Most patients with delayed visits complained that their doctor had advised them to wait and see, without any attempt to relieve their symptoms. Fast referral fast to a specialist in orofacial pain or oral surgery may help maximize the resolution of neuropathy, by interrupting and reversing the cascade of traumatic events.[5,24] Many authors recommend the referral of injuries before 4 months but this may be too late for many peripheral sensory nerve injuries,[5] since the first few months may determine the degree of nerve healing.[4] This time would need to be very short, perhaps within 24 hours of the injury, in the cases of implant or endodontic-related injury.[20,25] Therefore, identifying risk factors affecting permanent neuropathy would help clinicians to refer patients with neuropathic symptoms at the best possible time.

The panoramic view could provide gross information on involvement of IANI, demonstrating the loss of the lamina dura of the inferior alveolar nerve (IAN) canal, impingement of implant fixtures, and overfilling of endodontic materials into the IAN canal. However, in the case of LNI, and sometimes of mental nerve injury (MNI), the panoramic view does not provide proper information regarding nerve damage. CBCT scanning might be an alternative option,[26] but several papers have reported the weakness of CBCT evaluation in identifying the canal, resulting in poorer sensitivity and specificity.[27,28] In this study, however, there were 14 positive signs of nerve damage in CBCT, while there were 46 cases of no sign in the panoramic view. Thus, using CBCT may not be a routine procedure to assess the extent of nerve damage, but it could be necessary if the panoramic image fails to detect signs of nerve damage.

If a nerve injury is suspected, the clinician should perform a basic neurosensory examination of the neuropathic area and ascertain whether or not the patient is experiencing pain, altered sensation, or numbness.[4] In this study, reduced sensation in the pinprick test (hypoalgesia) was statistically significantly more frequent in the persistent group than in the transient group. Sensory loss is a universal response to nerve damage,[10] but hypoalgesia, in assessing sensory signature, was not predominant in the persistent group. In the comparison about sensory signature, allodynia showed statistically significance in the persistent group, compared to the transient group (Table 5). After the nerve injury, reactive changes centrally produce abnormal neural function. Allodynia (pain evoked by innocuous stimuli), and hyperpathia (anexplosive, abnormal pain that outlasts a stimulus) would indicate altered activity of peripheral nerves and their central pathway.[4] Therefore, a combination of dull sensation, allodynic and hyperpathic responses in a neurosensory examination could serve as an outcome predictor for the likelihood of permanent neuropathy. In this study, Nagelkerke's R^2, which represents the power of explanation of the model,[29] was 0.607. As scores of Nagelkerke's R^2 above 0.5 would indicate a strong association with the group.[30] Our value of 0.607 is indicatative of a strong association with the persistent group. To our knowledge, this is the first study to assess the difference in patient profiles between the transient and persistent groups. Based on this study, further investigations with larger study populations are warranted.

An ideal model for studying the development of chronic traumatic neuropathic pain, and establishing predictive factors for the condition, would include preoperative and postoperative assessment of psychological and neurophysiological factors, detailed intraoperative data on handling of tissue and nerves, and detailed early and late postoperative pain data, as well as a thorough clinical investigation to exclude other causes of the chronic pain state.[10] In this study, psychological evaluation was not performed. Considering the risk factors for postsurgical pain, psychological evaluation should be included in future studies.

REFERENCES

1. Woda A. Painful posttraumatic trigeminal neuropathy: a recently recognized entity. J Orofac Pain 2013;27:97-98.
2. Ryu JW, Kwon JS. Dysesthesia after tooth extraction and implant surgery reported by dentists. Korean J Oral Med 2007;32:263-272.
3. Merrill RG. Prevention, treatment, and prognosis for nerve injury related to the difficult impaction. Dent Clin North Am 1979;23:471-488.
4. Renton T. Prevention of iatrogenic inferior alveolar nerve injuries in relation to dental procedures. Dent Update 2010;37:350-362, 354-356, 358-360 passim.
5. Renton T, Yilmaz Z. Profiling of patients presenting with posttraumatic neuropathy of the trigeminal nerve. J Orofac Pain 2011;25:333-344.
6. Benoliel R, Zadik Y, Eliav E, Sharav Y. Peripheral painful traumatic trigeminal neuropathy: clinical features in 91 cases and proposal of novel diagnostic criteria. J Orofac Pain 2012;26:49-58.
7. Park JW, Choung PH, Kho HS, Kim YK, Chung JW. A comparison of neurosensory alteration and recovery pattern among different types of orthognathic surgeries using the current perception threshold. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2011;111:24-33.
8. Kraemer HC. Evaluating medical tests: objective and quantitative guidelines. Newbury Park (CA): Sage Publications; 1992.
9. Hillerup S. Iatrogenic injury to the inferior alveolar nerve: etiology, signs and symptoms, and observations on recovery. Int J Oral Maxillofac Surg 2008;37:704-709.
10. Kehlet H, Jensen TS, Woolf CJ. Persistent postsurgical pain: risk factors and prevention. Lancet 2006;367:1618-1625.
11. Jerjes W, Swinson B, Moles DR, et al. Permanent sensory nerve

impairment following third molar surgery: a prospective study. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2006;102:e1-e7.
12. Osborn TP, Frederickson G Jr, Small IA, Torgerson TS. A prospective study of complications related to mandibular third molar surgery. J Oral Maxillofac Surg 1985;43:767-769.
13. Wofford DT, Miller RI. Prospective study of dysesthesia following odontectomy of impacted mandibular third molars. J Oral Maxillofac Surg 1987;45:15-19.
14. Ziccardi VB, Steinberg MJ. Timing of trigeminal nerve microsurgery: a review of the literature. J Oral Maxillofac Surg 2007;65:1341-1345.
15. Benoliel R, Birenboim R, Regev E, Eliav E. Neurosensory changes in the infraorbital nerve following zygomatic fractures. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2005;99:657-665.
16. Mason DA. Lingual nerve damage following lower third molar surgery. Int J Oral Maxillofac Surg 1988;17:290-294.
17. Wismeijer D, van Waas MA, Vermeeren JI, Kalk W. Patients' perception of sensory disturbances of the mental nerve before and after implant surgery: a prospective study of 110 patients. Br J Oral Maxillofac Surg 1997;35:254-259.
18. Kraut RA, Chahal O. Management of patients with trigeminal nerve injuries after mandibular implant placement. J Am Dent Assoc 2002;133:1351-1354.
19. Hillerup S, Jensen R. Nerve injury caused by mandibular block analgesia. Int J Oral Maxillofac Surg 2006;35:437-443.
20. Grötz KA, Al-Nawas B, de Aguiar EG, Schulz A, Wagner W. Treatment of injuries to the inferior alveolar nerve after endodontic procedures. Clin Oral Investig 1998;2:73-76.
21. Jääskeläinen SK, Teerijoki-Oksa T, Virtanen A, Tenovuo O, Forssell H. Sensory regeneration following intraoperatively verified trigeminal nerve injury. Neurology 2004;62:1951-1957.
22. Bataineh AB. Sensory nerve impairment following mandibular third molar surgery. J Oral Maxillofac Surg 2001;59:1012-1017.
23. Hillerup S. Iatrogenic injury to oral branches of the trigeminal nerve: records of 449 cases. Clin Oral Investig 2007;11:133-142.
24. Susarla SM, Lam NP, Donoff RB, Kaban LB, Dodson TB. A comparison of patient satisfaction and objective assessment of neurosensory function after trigeminal nerve repair. J Oral Maxillofac Surg 2005;63:1138-1144.
25. Khawaja N, Renton T. Case studies on implant removal influencing the resolution of inferior alveolar nerve injury. Br Dent J 2009;206:365-370.
26. Friedland B, Donoff B, Dodson TB. The use of 3-dimensional reconstructions to evaluate the anatomic relationship of the mandibular canal and impacted mandibular third molars. J Oral Maxillofac Surg 2008;66:1678-1685.
27. Tantanapornkul W, Okouchi K, Fujiwara Y, et al. A comparative study of cone-beam computed tomography and conventional panoramic radiography in assessing the topographic relationship between the mandibular canal and impacted third molars. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2007;103:253-259.
28. Tantanapornkul W, Okochi K, Bhakdinaronk A, Ohbayashi N, Kurabayashi T. Correlation of darkening of impacted mandibular third molar root on digital panoramic images with cone beam computed tomography findings. Dentomaxillofac Radiol 2009;38:11-16.
29. Pace NL, Eberhart LH, Kranke PR. Quantifying prognosis with risk predictions. Eur J Anaesthesiol 2012;29:7-16.
30. Greiner M, Pfeiffer D, Smith RD. Principles and practical application of the receiver-operating characteristic analysis for diagnostic tests. Prev Vet Med 2000;45:23-41.