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Signs and symptoms, quality of life and psychosocial data in 1331 post-traumatic trigeminal neuropathy patients seen in two tertiary referral centres in two countries

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Abstract

Background: Post-traumatic trigeminal neuropathy (PTN) is a disturbance of function or pathological change of the trigeminal nerve branches following trauma and has an important impact on patient's quality of life (QoL).

Objectives: To provide diagnostic data on PTN and illustrate differences in aetiology, injured nerve, pain distribution, sensory profile and QoL between PTN subgroups.

Methods: 1331 patients with painful or non-painful PTN were retrospectively reviewed in two centres, extracting demographic data, time and cause of trauma, clinical findings including signs and symptoms, basic neurosensory testing, imaging modalities, treatments, and QoL or psychosocial assessment.

Results: More females were represented (70%) than males. The inferior alveolar nerve was most frequently damaged (60%) followed by the lingual nerve (28%). Wisdom teeth removal was considered the main cause (48%). Pain was reported in 63% of patients and pain frequency increased with age without clinically significant gender differences. Numbness was reported in 50% of PTN patients. Neurosensory testing showed larger affected dermatome involvement in persistent injuries, with no differences between the non-painful and painful PTN groups. Patient clustering indicated different sensory profile distributions when stratified according to aetiology or affected nerve branch. High interference with lifestyle was reported (78%), and patients suffering from painful PTN had worse QoL and psychosocial outcomes.

Conclusion: Patients with painful PTN had different clinical profiles and lower QoL scores than those with non-painful PTN. Sensory profiles may provide important prognostic and therapeutic information; however, more research is needed to assess the clustering procedure and link these clusters to therapeutic guidelines.

KEYWORDS

diagnosis, neuropathic pain, quality of life, trigeminal nerve, trigeminal nerve disorder

1 | INTRODUCTION

Neuropathic pain following trigeminal nerve injury (TNI) is a chronic pain condition that is the most problematic consequence of dental or oromaxillofacial surgical procedures with major medico-legal implications.[1] Painful post-traumatic trigeminal neuropathy (PPTN) has been defined in the current International Classification for Headache Disorders as trigeminal pain caused by major or minor trauma, chemical or thermal aggression, or radiation and is supported by a set of criteria that should be fulfilled to address this definition. In the recently published International Classification of Orofacial Pain (ICOP), PPTN has been slightly renamed to post-traumatic trigeminal neuropathic pain (PTNP).[2] Definitions and criteria of pain syndromes within the trigeminal system remain a matter of debate, and there has been difficulty discriminating among several entities that are summarised in Table S1.[3] Persistent dentoalveolar pain has very similar diagnostic criteria as PTNP.[4] Redundant terminology includes phantom tooth pain, painful neuropathy (non-traumatic) and atypical odontalgia. There is also an ongoing discussion regarding chronic post-surgical pain, which in many cases may share the same underlying pathophysiological process as PTNP.[5] In this study, we refer to the broader term 'post-traumatic trigeminal neuropathy (PTN)' to describe a painful or non-painful post-traumatic trigeminal neuropathy. When addressing painful post-traumatic trigeminal neuropathy, we use PTNP, the new name introduced by the ICOP.

Post-traumatic trigeminal neuropathy is relatively rare in dentistry (4%-5%) compared with other common general surgical procedures in which 20%-45% of patients experience persistent pain after surgical limb amputation, thoracotomy or breast surgery. Trauma and various dental and oral-maxillofacial procedures carry the risk of PTN, which can present in numerous ways ranging from loss of sensibility without any pain to severe neuropathic pain. Unfortunately, after nerve injury has occurred, high conversion rates to permanent neuropathy have been reported.[6] Surgical and medical treatment options for PTN often result in disappointing outcomes, rendering both the patient and practitioner dissatisfied and frustrated. Consequently, such complications can decrease the patient's quality of life (QoL) and lead to medico-legal action.[7,8] We presume that the impact of PTN on patients is underestimated and should be further studied and objectified. In addition, comparisons in the past were made among the various aetiologies or affected nerve branches without stratification according to sensory profile. From recent literature, we understand the need and importance of paying more attention to these profiles, as they may correlate with the underlying pathogenesis and may better predict treatment response.[9] It is also likely that QoL differs among these profiles and consequently should be further analysed as well.

The aim of this study was to provide diagnostic data on a large cohort of PTN patients and analyse differences in aetiology, injured nerve branches, pain distributions and QoL between subgroups. Included patients were all seen in two tertiary oro-facial pain centres, one in Belgium and one in the United Kingdom (UK). Patients were stratified according to painful and non-painful PTN and according to persistency of the neuropathy. Finally, subgroups of PTNP patients were constructed according to their sensory profile, which allowed for sub-analysis.

2 | MATERIALS AND METHODS

2.1 | Patient selection and data extraction

The study protocol was approved by the Ethical Committees of each centre with reference numbers S62333 (UZL), IRAS 145487 and 14/LO/0500 (KCL). The data were registered in a new database named TrigNerVeBeUK (TNVBUK). Patient records between January 2010 and October 2018 were screened for post-traumatic, including iatrogenic, injury to branches of the trigeminal nerve seen at the Department of Oral & Maxillofacial Surgery at UZ Leuven (UZL), Belgium, and the Department of Oral Surgery at King's College London (KCL), UK. Inclusion criteria were presentation with post-traumatic injury of the trigeminal nerve or its branches with a clinical or radiological diagnosis of neurosensory deficit (NSD) in the distribution of the trigeminal nerve. According to the ICHD-3 and recent ICOP criteria, only patients were included if there was a temporal relationship between the symptoms and the traumatic event and if the symptoms occurred within a neuroanatomically plausible area. Traumatic events that were considered included: facial trauma, local anaesthesia administration, tooth extraction (non-wisdom tooth extraction), implant placement, endodontic treatment and wisdom tooth surgery. Patients were considered to have persistent PTN if they continued experiencing symptoms for more than 3 months after the trauma occurred. This is in line with the definitions from International Association for the Study of Pain for chronicity after surgery and trauma.[10] Patients were excluded when the deficit presented in a region other than the trigeminal nerve. Patients suffering from transient NSDs after orthognathic surgery were also excluded. Information retrieved from the records included demographic data, time and cause of trauma, signs and symptoms, basic neurosensory testing, preferred imaging modalities in relation to the injury, treatments, and QoL and/or psychosocial assessment by questionnaires as stated below. Missing data were handled by listwise deletion to obtain conservative results.

2.2 | Neurosensory testing

Neurosensory testing (NST) was based on previously described methods.[11-13] Parameters included the approximate size of the affected dermatome, light touch discrimination (LTD), sharp/blunt discrimination (SBD), moving-point discrimination (MPD) and response to hot and cold stimuli. The affected dermatome was defined as the area in which the pain complaint occurred and/or in which the neurosensory deficiency was diagnosed. Affected dermatome size was expressed in percentage: 0% indicated that no neuropathic area was measurable; 100% indicated that the

complete dermatome of the injured nerve was affected. The pain was assessed on a visual analogue scale (VAS) ranging from 0 (no pain) to 10 (worst pain imaginable) or on a scale ranging from 0 (no pain) to 100 (worst pain imaginable). Responses to the other parameters (LTD, SBD, MPD and thermal tests) were categorised as follows: no response, little or reduced sensation, normal sensation, elevated sensation.

2.3 | Sensory profiles and clustering

Based on symptoms reported during history taking and clinical findings including NST, patients were further stratified into the following sensory profiles: pain without a sensory deficit, sensory loss with or without pain, mechanical hyperalgesia or allodynia and thermal hyperalgesia or allodynia or combinations of the aforementioned profiles. Next, three clusters of patients were constructed focusing on PTNP based on the basic neurosensory testing and patient descriptors. Cluster one represented patients with self-reported pain and numbness without thermal or touch-evoked complaints and a predominant sensory loss on neurosensory tests. Cluster two represented patients reporting thermal symptoms including thermal hyperalgesia or allodynia (hereafter referred to as thermal hyperesthesia) confirmed by basic neurosensory testing, and cluster three represented patients reporting touch-evoked symptoms and have confirmed mechanical hyperalgesia or allodynia (hereafter referred to as mechanical hyperesthesia) on neurosensory testing. Additional analyses looked at the effects of clustering on the following parameters: injured nerve, cause, age and gender, transient or persistent injury, duration of injury, interference with lifestyle, and results from QoL and psychosocial questionnaires.

QoL and psychosocial questionnaires

The used instruments and their characteristics are summarised in Table S2. A general health-related QoL assessment was measured in both centres by the EuroQol (EQ5D-5L) questionnaire. All other questionnaires were only administered in the UK centre (KCL). The EQ5D-5L assesses five domains including mobility, self-care, usual activities, pain/discomfort and anxiety/depression on a 5-point ordinal scale (0: no problems; 1: slight problems; 2: moderate problems; 3: severe problems; 4: extreme problems). Patients indicated their self-rated health on a VAS from 0 (worst) to 100 (best health they could imagine). Interference with lifestyle and daily activities was also registered from the patient records.

Patients seen at KCL were asked to complete several questionnaires measuring psychosocial impact. A subsequent analysis was performed to assess differences between sensory profiles and clusters. No assessment of differences between transient and persistent injury was executed due to the low number of questionnaires performed in patients with transient injuries. The 9-item Patient Health Questionnaire (PHQ-9), testing the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) criteria for depression, was rated on a 4-point scale ranging from 0 (not at all) to 3 (nearly every day) resulting in a total score from 0 to 27. Mild depression was considered from a score of 5, moderate from 10, moderately severe from 15 and severe from 20. Anxious symptoms were assessed with the 7-item Generalized Anxiety Disorder Questionnaire. Responses were recorded in the same way as PHQ-9, resulting in a total score ranging from 0 to 21. Higher scores are indicative of anxiety disorder or mood. A multidimensional assessment of oral health-related quality of life (OHrQoL) was performed by using the Oral Health Impact Profile, a tool that determines functional limitations, physical pain, psychological impact and disability, social disability and handicap. Fourteen items were scored on a scale from 0 (never) to 4 (very often), and an overall score ranging from 0 to 56 was calculated.

The Multidimensional Scale of Perceived Social Support assessing the perception of support by family, friends and a significant other was measured by 12 items on a 7-item scale (0: very strongly disagree; 7: very strongly agree). Subscores for family, friends and a significant other were calculated by a mean. The total score was calculated and divided by 12. Higher scores indicate high levels of support perceived. A post-traumatic stress disorder screener questionnaire (PCL-6) was calculated by a total sum of six items scored on a 5-item scale (1: not at all; 5: extremely). A positive score for a post-traumatic stress disorder was considered as a total sum of 14 or higher. Pain questionnaires included the Short-Form McGill Pain Questionnaire-2, which scores neuropathic pain symptoms on an 11-point numeric rating scale. The overall score was calculated as a mean of the 22 responses. Higher scores represent a more severe presentation. The painDETECT questionnaire is a well-known assessment tool for neuropathic pain complaints. It includes 11-point numerical rating scales dedicated to the evaluation of a patient's reported current pain level and its strongest and average levels during the past month. This questionnaire also contains nine other items, of which seven are related to sensory responses and two are related to the temporal and spatial characteristics of the pain pattern. Sensory responses (burning, allodynia, thermal sensitivity, numbness, attacks, pressure pain) are scored on a 6-point scale (0: never; 1: hardly noticed; 2: slightly; 3: moderately; 4: strongly; 5: very strongly). A total score was calculated according to the author's directives. The Pain Self-Efficacy Questionnaire was used to assess the patient's confidence in performing activities (work, leisure, household chores) despite the symptoms. A 7-point scale ranging from 0 (not at all confident) to 6 (completely confident) was recorded, and a total score from 0 to 60 was calculated. The Chronic Pain Acceptance Questionnaire measures acceptance of pain using 8 items on a 7-point scale (0: never true; 6: always true). Subscores were calculated for pain willingness and activity engagement. Higher scores indicate a higher level of acceptance. The Pain Catastrophizing Scale assesses an exaggerated negative orientation towards painful stimuli and is indicative of coping skills. Thirteen items are scored on a 5-item scale (0: not at all; 4: all the time) with a total score ranging from 0 to 52. Three subscales are constructed measuring rumination, magnification and helplessness.

2.4 | Statistical analysis

All data were assessed by a certified statistician using SAS version 9.3 (SAS Institute) and SPSS version 25.0 (IBM Corp). Means, standard deviations (SDs), range and frequencies were calculated. The chi-square test was used to compare non-parametric frequencies. In models applied with aggregated data from Belgium and the UK, centres were added as a fixed effect, and it was determined if the relationships were country-dependent. Pearson's correlation was used to measure the relationship between pain VAS scores and age. The chi-square test was used to compare gender and pain VAS scores as well as to compare NST parameters between groups, and Bonferroni correction was applied for multiple comparisons. Analysis of variance with the Games-Howell post hoc test was used to detect differences between the questionnaire mean scores of the non-painful versus painful PTN groups and transient versus persistent PTN. Analysis of NST measures, and psychosocial and QoL questionnaires among clusters was not performed because the sample size of the individual groups was too low for meaningful comparisons. P-values less than 0.05 were considered statistically significant.

3 | RESULTS

3.1 | General

A total of 1331 patients were included in this study: 926 (70%) females and 405 (30%) males with a mean age of 46 years (SD: 14.6, range: 13-91). No significant differences in age or gender were observed among clusters or institutes. We included 958 patients from KCL and 373 patients from UZL.

Most patients were referred by an oral and or maxillofacial surgery specialist (147; 40%) or by a dentist (112; 30%). The injury was most frequently caused by a dentist (326; 44%) or specialist (317; 42%). The mean duration of symptoms before presentation was 112 days (SD: 238, range: 0-2801). The inferior alveolar nerve (IAN) was affected in 806 (60%) patients, the lingual nerve (LN) in 371 (28%), and the maxillary nerve (MN) in 218 (16%) patients. Fifty (4%) patients experienced injury to both the lingual nerve and inferior alveolar nerve. In 21 (2%) patients, an injury to both the IAN and MN was seen (Figure S1). No significant difference was noted in the presence of inferior alveolar nerve injury among clusters. Lingual nerve injuries, however, significantly differed between cluster one compared to clusters two and three ($P < .05$), being more frequent in cluster one. Maxillary nerve injuries were more frequent in clusters one and two compared to cluster three. The most frequent cause of trigeminal nerve damage was third molar surgery accounting for 519 (48%) patients followed by dental implants in 146 (13%), extractions (non-third molar) in 136 (13%), local anaesthesia in 125 (12%), endodontic treatment in 86 (8%) and trauma in 74 (7%) patients (Figure S1). A similar distribution was seen among clusters. Frequencies of the affected branch and aetiology were comparable between the two centres.

3.2 | Symptoms

Pain was the most reported symptom in 837 (63%) patients, followed by numbness in 672 (50%) (Table 1). Paresthesia was reported in 491 (37%) patients, and burning sensations were present in 156 (12%). Table S3 provides an overview of the three most reported symptoms, their frequency and co-existence. Forty per cent of patients with pain also complained of numbness. 43% reported both pain and paresthesia. Two hundred and seven patients (15.6%) described a combination of pain, paresthesia and numbness. VAS pain scores ranging from 0 to 100 increased with age ($P < .0001$) with a mean of 38 (SD: 35.1). Females reported higher VAS scores with a mean of 46.00 (SD: 14.81 [13.00-91.00]) compared to males with a mean of 45.50 (SD: 14.81 [19.00-85.00]) ($P = .0005$). Forty-one per cent of all patients reported a score

TABLE 1 Most frequently reported symptoms by post-traumatic trigeminal neuropathy patients and results of basic neurosensory testing

Reported signs and symptoms	N			%
Pain	837			63
Numbness	672			50
Paresthesia	491			37
Burning sensations	156			12
Neurosensory test results	**n/N**	**%**	**Mean (%)**	**SD**
Affected dermatome extra-oral	454	—	56	35
Affected dermatome intra-oral	371	—	57	39
Light touch test				
No sensation	65/200	33		
Little/reduced sensation	59/200	30		
Normal sensation	29/200	15		
Elevated sensation	19/200	10		
Extra-oral sharp-blunt discrimination				
No sensation	39/187	21		
Little/reduced sensation	42/187	23		
Normal sensation	60/187	32		
Elevated sensation	15/187	8		
Intra-oral sharp-blunt discrimination				
No sensation	18/81	22		
Little/reduced sensation	24/81	30		
Normal sensation	15/81	19		
Elevated sensation	7/81	9		
Moving-point discrimination				
No sensation	40/177	23		
Little/reduced sensation	25/177	14		
Normal sensation	22/177	12		
Elevated sensation	1/177	1		
Thermal discrimination				
No sensation	12/174	7		
Little/reduced sensation	14/174	8		
Normal sensation	22/174	13		
Elevated sensation	16/174	9		

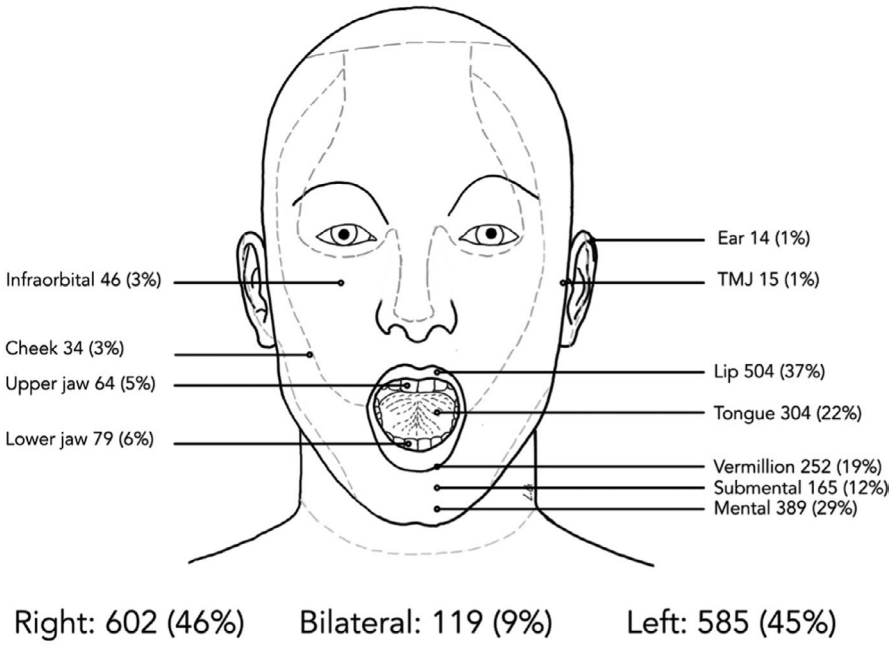

FIGURE 1 Symptom distribution. Most frequently involved area is situated in the mental area

of 50 or higher. Patients with persistent injury had significantly higher VAS scores than those with transient injury (4.35 [SD: 3.51] vs 0.85 [SD: 2.23], respectively, $P < .001$).

Symptoms were most frequently reported in the lower lip and chin region (Figure 1). Some patients had complaints at the level of the temporomandibular joint or ear. The tongue was affected in 304 (22%) patients, and bilateral symptoms were noted in 119 (9%). Most patients complained of constant symptoms (87%), whereas 13% had intermittent symptoms. Reported symptoms were comparable between the two institutes.

3.3 | Neurosensory tests

The mean percentage of the affected extra-oral dermatome was 56% (SD: 35) and was comparable between the two centres. Intra-oral, a mean affected dermatome was noted of 57% (SD: 39). Mapping of the affected percentage of the dermatome showed a significantly larger affected area when persistent injury was present (mean: 59.61%, SD: 34.183) comparing to a transient injury (29.45%, SD: 34.179; $P < .001$). The same was true regarding involvement of the intra-oral dermatome (59.81%, SD: 33.018% vs 23.93%, SD: 32.236; $P < .001$). NST results are summarised in Table 1. More patients showed an abnormal response to NST when the injury was considered persistent compared to transient NSD ($P < .05$). When comparing painful to non-painful PTN, no significant differences in NST outcomes were identified.

3.4 | Sensory profiles

After clustering PTPN patients, 420 (43.03%) patients were assigned to cluster one (sensory loss with pain), 247 (25.31%) to cluster two (thermal hyperesthesia) and 309 (31.66%) to cluster three (mechanical hyperesthesia). A total of 82 (8.40%) patients were assigned to both clusters one and three, 61 (6.25%) to clusters one and two and 46 (4.71%) to clusters two and three, and 108 (11.07%) patients were assigned to all three clusters (Figure 2).

Following significant differences ($P < .05$) were observed when examining the distribution of sensory profiles between the different affected nerve branches and aetiologies. We observed a higher representation of LN injuries in cluster one compared to IAN or MN injuries (Figure 3). MN injuries were more prevalent in cluster three, and affected branches were more evenly distributed in cluster two. Among the different aetiologies, there was a higher representation

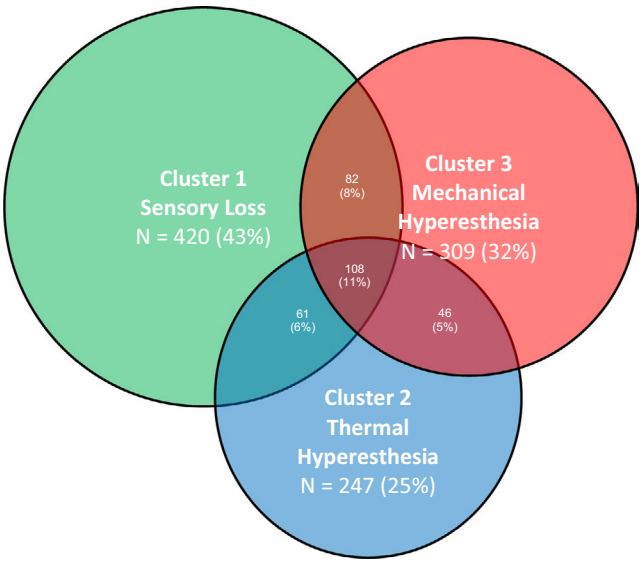

FIGURE 2 Clusters of sensory phenotype frequency and overlap for post-traumatic trigeminal neuropathic pain. Sizes of circles are to scale; overlaps are not to scale

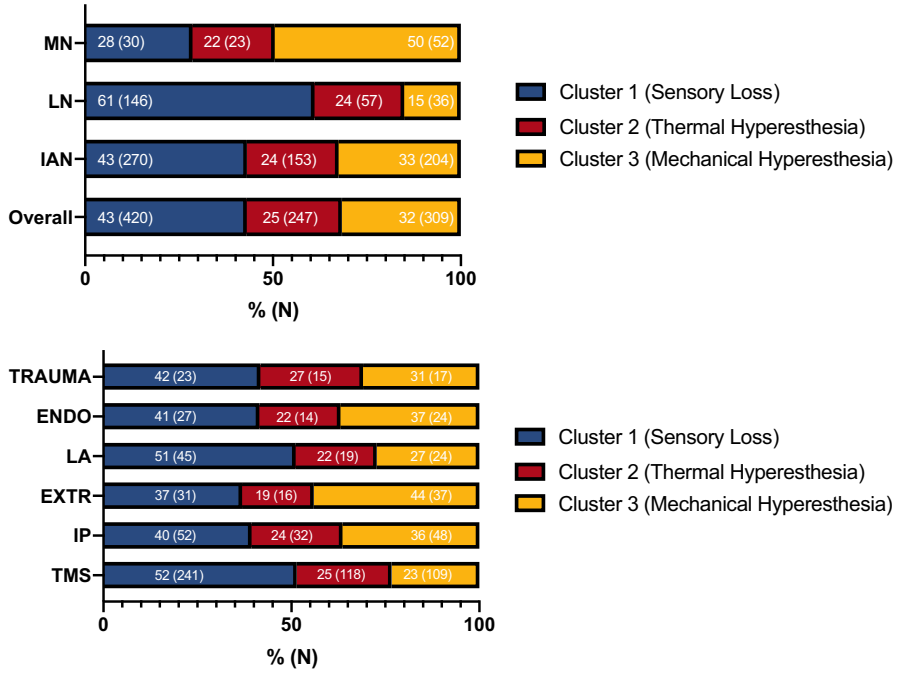

FIGURE 3 Distribution of the three clusters within the injured nerve branch and within aetiologies

of patients suffering injury after third molar surgery or local anaesthesia in cluster one. Extraction-induced injuries or those incurred after implant placement or endodontic treatment were most frequent in cluster three. An equal distribution among aetiologies was seen in cluster two (Figure 3).

3.5 | QoL and psychosocial impact

In total, 607 patients reported interference with their lifestyle (77.7%), whereas 174 patients reported no interference. More detailed data on interference are reported in Figure 4. Most interference was reported for eating (420; 60.3%), speech (294; 42.9%), kissing (224; 33.6%), drinking (174; 25.7%) and sleeping (129; 18.5%). Clusters significantly differed for speech ($P = .021$), eating ($P = .024$), drinking ($P < .001$), kissing ($P < .001$) and sleeping ($P = .006$). More interference was noted if the patient had mechanical hyperesthesia or was categorised in multiple clusters. In addition, compared to patients with transient injury, more patients with persistent injury complained of lifestyle interference (76.4% vs 7.6%; $P < .05$).

The main results from all questionnaires are illustrated in Tables S4-S6. All EQ5D parameters were significantly different between painful

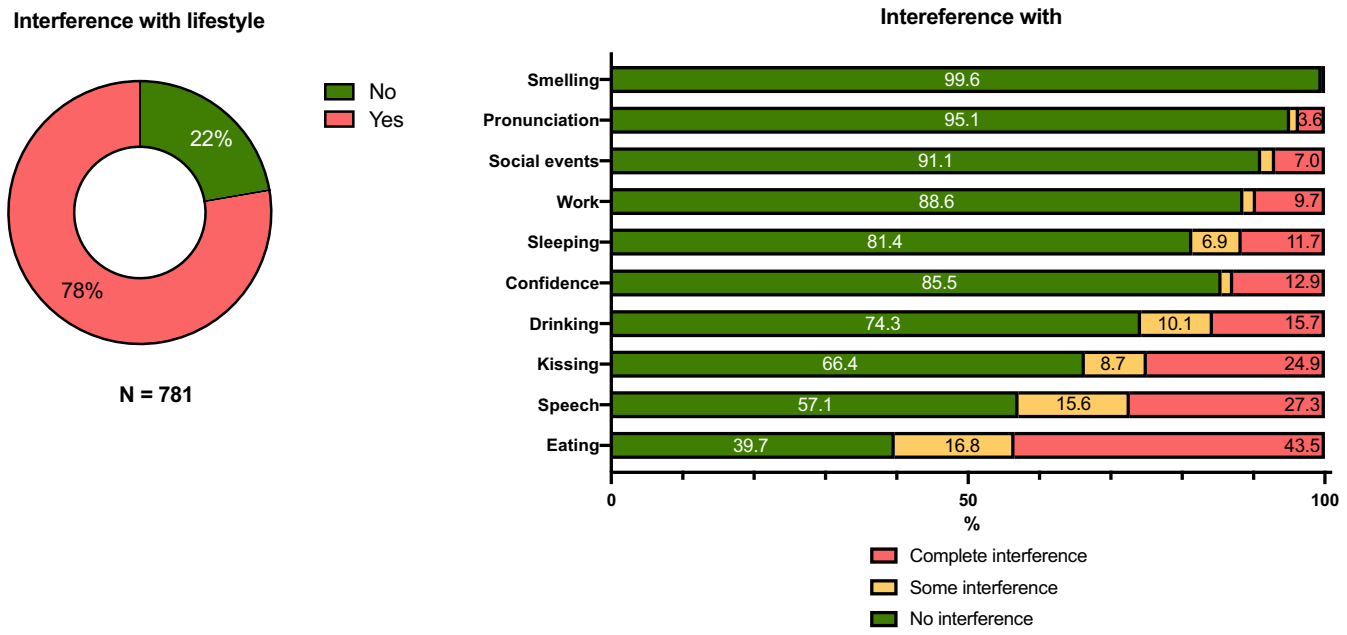

FIGURE 4 Self-reported interference of lifestyle of Post-traumatic trigeminal neuropathy patients and stratified for subdomains indicating degree of interference

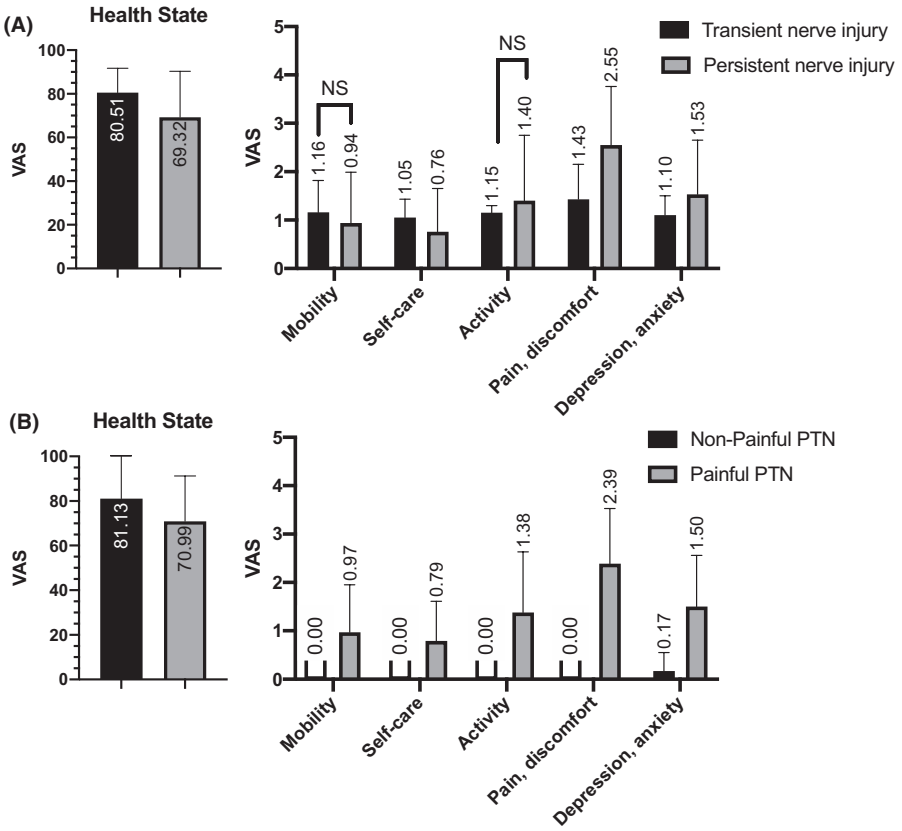

FIGURE 5 Quality of life domains and self-perceived health state measured by the EQ5D-5L questionnaire. Comparison between transient and persistent nerve injuries (A) as well as non-painful versus painful post-traumatic trigeminal neuropathy (B). NS, not significant. Open-ended boxes indicate a value of zero with standard deviation of zero. Standard deviations are indicated

and non-painful PTN, illustrating worse QoL measures if painful PTN is present (Figure 5). EQ5D measures between transient and persistent injury showed significantly worse outcomes for activity, pain, depression and health state in patients with persistent injury. Interestingly, self-care was perceived to be worse in patients with a transient injury ($P < .05$). Mobility and activity scores between patients with persistent or transient injury were not significantly different.

Patients with PTNP had significantly higher scores for anxiety and depression with less perceived social support compared to those with non-painful PTN. The mean PCL-6 score was positive for post-traumatic stress disorder in PTNP patients, but this was not the case in the non-painful PTN group. OHrQoL was considered worse in PTNP with a mean score of 30 (SD: 14.9). No significant difference was found in the total score on pain acceptance between both groups. However, pain willingness was significantly lower for the PTNP group. PainDETECT mean VAS scores were all significantly higher in PTNP patients. A neuropathic component was unclear for both groups based on the mean sum score of the 6-point ordinal scales. Other instrument outcomes were not significantly different between painful and non-painful PTN or between transient and persistent PTN due to the low sample sizes.

4 | DISCUSSION

4.1 | General

There is a lack of clarity regarding the diagnostic criteria for NSD after trigeminal nerve injury, and many studies have only assessed axis one and ignored psychological and physiological features.[14] Recommendations for somatosensory testing and the reliability and variability assessment of NSDs in the trigeminal system also vary from very simple assessments to using complex quantitative sensory testing (QST) in the German Research Network.[12,15] Previous studies have well established the frequencies of causes for trigeminal nerve injury as well as the distribution of affected trigeminal nerve branches.[6] The incidence of lingual nerve injury has remained static in the UK over the last 30 years but is increasing in the United States, as is the incidence of inferior alveolar nerve injury in the UK, the latter being due to implant surgery and endodontic therapy.[16] No definitive data are available for Belgium on this topic.

Women were more represented than men in this study, in accordance with previous studies.[6,8,17] The fact that oral and maxillofacial surgeons and dentists are the main referrers but also the practitioners that most frequently cause the injuries is not surprising if we consider the anatomy of the inferior alveolar and lingual nerve. What remains striking is the duration of symptoms before the patient is seen at a tertiary centre. A mean duration of 112 days means a referral delay beyond what is considered the therapeutic window of opportunity of 3 months after the injury occurs.[18] Within this window of opportunity, surgical intervention is most likely to be successful.[19,20] In addition, the phenomenon of peripheral and central sensitisation can potentially be arrested within this period.

Injury to the third division of the trigeminal nerve was most frequent, with the IAN being affected in 60% of all cases, in accordance with the literature.[6] A small percentage of patients experienced

injury to more than one branch. Inferior alveolar nerve injuries were equally distributed within the three constructed clusters; however, lingual nerve injuries were more frequent in cluster one, indicating a shift in symptom patterns for these patients.

Third molar surgery was the most frequent cause of nerve injury (48%), followed by dental implants (13%). We believe that the frequency of dental implant injuries is rising due to the growing demand, but insufficient scientific data are currently available to prove this point. Local anaesthesia injuries, which were the third most frequent injury in our population, can occur by needle perforation and subsequent haemorrhage can cause compression in and around the nerve.

4.2 | Symptoms

Pain was the most reported symptom in 63% of patients followed by numbness or sensory loss in 50%, paresthesia in 37% and burning sensation in 12%. Forty per cent of patients with pain also complained of numbness. 43% reported both pain and paresthesia. Two hundred and seven patients (15,6%) described a combination of pain, paresthesia and numbness. Some patients experienced symptoms on both sides (9%). This group included patients with a bilateral injury as well as those experiencing radiation, referred pain or mirror pain on the contralateral side. Older patients and females reported higher VAS pain scores; however, the difference was statistically but not clinically significant. A total of 41% of all patients reported VAS scores of 50 or higher, in accordance with previous reports of spontaneous pain in 20%-40% of patients depending on the injured branch.[8] Symptom distribution showed a high percentage of symptoms in the tongue compared with registered lingual nerve injuries, which may be explained by afferent cross connections at the peripheral and central levels. A small percentage experienced pain around the ear or temporomandibular joint, which receives trigeminal innervation; this can be attributed to referred pain and symptoms or comorbidity at the time of injury.

4.3 | Neurosensory tests

Qualitative sensory testing showed smaller affected dermatomes in patients suffering from a transient injury, and this was true for intra-oral and extra-oral dermatomes. The results are comparable to a previous study by Yilmaz et al and suggest that measuring the affected dermatome could aid in differentiating between transient and persistent injuries.[8] The results from different modality tests are variable, but more abnormal responses to light touch were seen in persistent injuries. In addition, we did not identify significant differences in NST results between painful and non-painful PTN, which raises the question of the usefulness of these tests. Recent reports comparing QST with qualitative sensory testing raised concerns about its diagnostic value in chronic stages.[21] With the current scientific knowledge, it remains difficult to identify a reliable and clinically feasible test. However, a combination of different modalities seems to have the highest predictive value and qualitative NSTs often remain the first choice in the clinic.

4.4 | Sensory profiles

Grouping patients into sensory profiles and clusters allows for a more clinically relevant approach towards these injuries. Attempts have been made to stratify patients presenting with neuropathic pain outside the trigeminal system.[22] Some reports found that QST did not distinguish between painful and painless neuropathies regarding small fibre function, but revealed higher mechanical pain ($P < .01$) and detection thresholds ($P < .05$) and lower mechanical pain sensitivity in the group of patients with painful neuropathies.[22,23] The authors identified three distinct sensory phenotypes in patients suffering from neuropathic pain, providing an algorithm to allocate individual patients to said phenotypes. All three phenotypes were present in diabetic polyneuropathy, peripheral nerve injury and post-herpetic neuralgia, but the frequencies differed.

Moreover, studies have shown the importance of clustering towards treatment response.[9,24] Those studies used QST according to the German Research Network on Neuropathic Pain. These tests, although very precise, remain clinically cumbersome and time-consuming. In this study, the patients were grouped according to their symptoms and results of basic NSTs. This method is relatively rough compared to a full QST, but allows insight into the different clinical presentations. However, concerns have been raised that qualitative sensory testing does not correlate well with QST.[21,25,26] More research will be needed to assess which QST parameters are most important in correctly assigning patients to these clusters. For application in a clinical setting, these tests must be easy to use and able to be performed in a limited time. This study provides an impetus for moving the clinical thinking framework in this direction.

In this study, most patients were assigned to a sensory loss phenotype (43%), followed by mechanical and thermal hyperesthesia. A rather large group of patients (11%) was assigned to all three clusters. A similar overall distribution of profiles was reported by Vollert et al in polyneuropathy cases where the sensory loss phenotype was predominant compared to small fibre neuropathy where gain-of-function phenotypes were noted.[23] When looking at different aetiologies or affected nerve branches, we observed a shift in distributions.[22] Thermal and mechanical hyperesthesia are especially represented in patients with maxillary nerve injuries. A possible explanation could be that nerve injuries of the maxillary branch are rather infrequent due to the fact that branching takes place higher up compared to the lingual and inferior alveolar nerve, making it less prone to injury. If an injury does occur, the impact is correspondingly higher. Also, a different fibre distribution or nerve architecture could add to the shift in sensory phenotype distribution. When looking at lingual nerve injuries, the sensory loss phenotype is more represented than mechanical or thermal hyperesthesia. One explanation could be the fact that the

lingual nerve is most frequently injured after third molar surgery, which was also a more represented aetiology in cluster one patients. Also, lingual nerve injury is most frequently damaged away from its peripheral endings before entering the tongue where larger fascicles are present.

4.5 | QoL and psychosocial impact

In the study of Castro et al, patients with persistent pain had higher levels of depression.[27] The authors found that disease severity was associated with higher limitations and that patients who had been treated had higher levels of depression possibly due to pain chronification. In this study, we found similar results. Additionally, self-care was perceived as worse in those with transient injuries, possibly because patients who are newly diagnosed with neuropathic pain have higher levels of anxiety of no improvement, which has been shown to be predictive of pain interference.[28] A limitation of this study was the use of the EQ5D-5L, which is non-specific for the oro-facial domain. Future studies could implement oral health-related QoL questionnaires to improve specificity for these measures.

Several studies have found that PTNP patients are more likely to have to quit work due to their chronic pain, which is associated with a substantial psychosocial burden, pain catastrophising and reduced QoL.[29-31] This study adds further evidence of psychosocial distress and decrease in function experienced by patients with PTNP.

The retrospective nature of this study was a major limitation, and as such, the results should be interpreted with caution. Missing data in subgroups did not allow for comparison of the QoL and psychosocial outcomes among clusters (some questionnaires were only completed by 103 (7.7%) patients in this study). In the future, the combination of these clusters and therapeutic guidelines can help re-establish oral function after PTNP. To allow these future analyses, a prospective cohort study has already begun and should provide answers in the following years.

It can be concluded that PTNP has a higher impact on QoL and psychosocial aspects than non-painful PTN. Sensory profiles represent different clinical presentations. Therefore, this study can be regarded as an incentive for grouping PTNP patients into sensory profiles and clusters.

5 | CONCLUSION

In this study, we presented results on clinical, QoL and psychosocial data from a large cohort of patients diagnosed with PTN seen at two tertiary centres in two countries. Patients suffering from PTNP had different clinical profiles compared to non-painful PTN and had lower QoL scores with a larger impact on psychosocial scales.

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CONFLICT OF INTEREST

The authors declare no financial or non-financial interest in the subject matter or materials discussed in this manuscript.

AUTHORS' CONTRIBUTION

F. Van der Cruyssen contributed to conception, design, data acquisition, analysis and interpretation drafted and critically revised the manuscript. F. Peeters contributed to data acquisition, analysis and interpretation and critically revised the manuscript. T. Gill contributed to data analysis, interpretation and critically revised the manuscript. A. De Laat contributed to conception, design and critically revised the manuscript. R. Jacobs contributed to conception, design, data interpretation and critically revised the manuscript. C. Politis contributed to conception, design, interpretation and critically revised the manuscript. T. Renton contributed to conception, design, data acquisition, data interpretation and critically revised the manuscript. All authors gave their final approval and agree to be accountable for all aspects of the work.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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