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# The benefit of surgical management in post-traumatic trigeminal neuropathy: a retrospective analysis

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*Abstract.* Post-traumatic trigeminal neuropathy (PTTN) is a known complication of common oral and maxillofacial procedures. The burden on the patient and society is often underestimated. This retrospective study included 29 patients with PTTN who underwent surgical treatment. Symptoms were differentiated, pre- and postoperatively, into neuropathic discomfort and loss of perceptive function. Clinical and patient-reported outcomes were recorded. The Brief Pain Inventory questionnaire was completed at the last follow-up. The effect of different variables was evaluated through subgroup analysis. The mean time interval between injury and surgery was 19 weeks. Overall, 20 patients (69%) showed improvement during a mean follow-up of 49 months. Neuropathic pain decreased in most patients (13/18; 72%) and two patients became pain-free. However, 16 patients reported persistent pain on the Brief Pain Inventory questionnaire. Medication use decreased postoperatively. Subgroup analysis showed a positive association between improvement and male sex (Fisher's exact test, $P = 0.033$), and between improvement and the buccal fat nerve wrapping procedure (Fisher's exact test, $P = 0.02$). In conclusion, surgery showed substantial benefit in the treatment of PTTN, even when neuropathic pain was present. The effect of different variables and the potential of buccal fat nerve wrapping should be evaluated further in future research.

Key words: traumatic trigeminal nerve injury; neuropathic pain; post-traumatic trigeminal neuropathy; nerve repair; surgery; treatment.

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Iatrogenic injury of the trigeminal nerve is a known complication of oral and maxillofacial surgery. Injury can be inflicted during common procedures like implant surgery and the removal of impacted lower third molars[1,2]. Mostly, the inferior alveolar nerve (IAN) and lingual nerve (LN) are at risk. Afterwards, patients complain of altered sensation (neurosensory disturbance), and neuropathic pain can develop. The International Classification of Headache Disorders third edition classifies this pain as ''painful post-traumatic trigeminal neuropathy''[3]. Most pain can be managed adequately with pain medication. However,

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neuropathic pain requires a different approach as it is a more vexatious type of pain. It is difficult to obtain complete resolution of symptoms, and pain recurrence is common. After 3 months, neuropathic pain becomes chronic and central sensitization often occurs[4]. Patients experience this type of pain as debilitating and it significantly affects their quality of life (QoL)[5]. Other neurosensory disturbances like hypoesthesia, anaesthesia, and dysesthesia should not be underestimated. Patients often report problems with speech, eating, and kissing[6]. These symptoms have an impact on relationships and bring a substantial psychological burden[7].

Post-traumatic trigeminal neuropathy (PTTN), whether or not painful, requires a holistic treatment approach. First of all, oral and maxillofacial practitioners should be aware of this complication and inform their patients properly before surgery[8]. When nerve injury occurs, it should be acknowledged. Treatment options and the prognosis should be discussed. Swift and adequate treatment is essential to obtain optimal results and prevent chronicity. Spontaneous recovery can occur, mainly within the first 3 to 6 months. Afterwards symptoms become permanent. Recovery is rare when symptoms persist for more than 1 year[9–11]. Pharmacological treatment consists of analgesics, opioids, and atypical pain medications such as antiepileptics, antidepressants, and benzodiazepines. The International Association for the Study of Pain recommends carbamazepine, duloxetine, pregabalin, and gabapentin as first-line treatment for neuropathic pain[12]. In selected cases, surgical nerve repair should be considered. Indications include suspected nerve transection, non-improving anaesthesia after 3 months, progressively decreasing sensation or increasing pain, and pain due to a neuroma, nerve compression, foreign body, or canal deformity[13].

The burden of PTTN on the patient and society should not be underestimated. PTTN often evokes feelings of anger and frustration, resulting in lawsuits against the practitioner. In oral and maxillofacial surgery, LN injury following third molar removal is the main cause of malpractice lawsuits[14]. The literature regarding the surgical management of PTTN is limited. Variables that affect the outcomes are still debated and the perfect time interval between injury and surgery remains controversial. Therefore, its treatment, including surgery, needs further investigation so that clinical guidelines can be produced.

The aim of this retrospective study was to evaluate the potential benefit of surgical management in patients with PTTN. Through subgroup analyses, the effects of different variables on the chance of improvement were examined.

## Materials and methods

This study is reported in accordance with the EQUATOR guidelines (Enhancing the Quality and Transparency of Health Research) and STROBE agreement (Strengthening the Reporting of Observational Studies in Epidemiology).

### Patient selection

This study formed part of a large retrospective cohort study for which ethical approval was obtained from the Ethics Committee of the University Hospital Leuven (S62333). It was performed in accordance with Good Clinical Practice standards and the Declaration of Helsinki. Inclusion criteria for this study were (1) confirmed diagnosis of PTTN, (2) surgical treatment, and (3) surgery and follow-up took place in the Department of Oral and Maxillofacial Surgery, University Hospitals Leuven, Belgium. Exclusion criteria were (1) implantation of neurostimulation devices, (2) cryotherapy, and (3) interventions involving the Gasserian ganglion. Patients were selected by analysing the patient records between 2013 and 2018. In total, 380 patients were diagnosed with PTTN at the tertiary referral centre of the Department of Oral and Maxillofacial Surgery, University Hospitals Leuven. Of these, 75 underwent surgical treatment. Further examination identified 29 patients who met the necessary eligibility criteria. The surgical intervention and follow-up took place between January 2005 and August 2019.

### Data collection

Data were extracted from the patient records, surgical reports, and medication prescriptions. These included demographic data, cause of injury, affected nerve, symptoms before and after the intervention, time interval between injury and surgery, intraoperative observations, surgical procedure, improvement, time of follow-up, and medication use.

Symptoms were differentiated into neuropathic discomfort and loss of perceptive function, and were assessed before and after the surgical intervention. Neuropathic discomfort included hyperesthesia, allodynia, paresthesia, hyperalgesia, and dysesthesia. A clear differentiation between neuropathic pain and dysesthesia was made. Loss of perceptive function included hypoesthesia, anaesthesia, and loss of taste. The intraoperative observations, procedure performed, and additional interventions were extracted from the surgical report. Decompression was further subdivided based on its nature. Follow-up took place during regular consultations. Due to the retrospective nature of this study, preoperative consultations and follow-up were not standardized.

Improvement was rated by examining scores of qualitative sensory testing, use of pain medication, and patient-reported outcomes. Improvement was subdivided on an ordinal scale, as follows: ‘worse’, symptoms were worse; ‘same’, symptoms were unchanged; ‘some’, symptoms had improved a little; ‘a lot’, symptoms had improved greatly; ‘complete’, complete resolution of the symptoms. Improvement of pain was classified as ‘same’, ‘less’, or ‘pain-free’. Improvement was evaluated according to the cause of injury and procedure performed. Medication intake was inspected before and after the surgical intervention. Drugs were further divided into five groups: analgesics, opioids, antidepressants, anti-epileptics, and benzodiazepines. The last follow-up assessment was conducted by phone or via email. The Brief Pain Inventory (Short Form) questionnaire (BPI) was completed at the last follow-up to assess residual pain levels and their impact on daily activities. This questionnaire was not conducted preoperatively.

### Statistical analysis

Descriptive statistics were used to analyse the collected data, including demographic data, different variables pre-, intra-, and postoperative, improvement after surgery, medication use, and BPI scores. One patient underwent two separate interventions. In the statistical analysis, she was considered under one study ID and improvement was evaluated after the second procedure. Loss to follow-up was addressed using the ‘last observation carried forward’ principle. A subgroup analysis was performed to examine the effect of different variables on improvement. Groups were divided based on sex, age ($<$50 years or $\geq$50 years), cause of injury, affected nerve, time interval until surgery ($<$3 months, $\geq$3 to $\leq$12 months, or $>$12 months), types of symptoms, the presence of neuropathic pain preoperatively, and the surgical procedure performed. Due to the small study population, improvement was considered a binominal variable (‘improvement’ or

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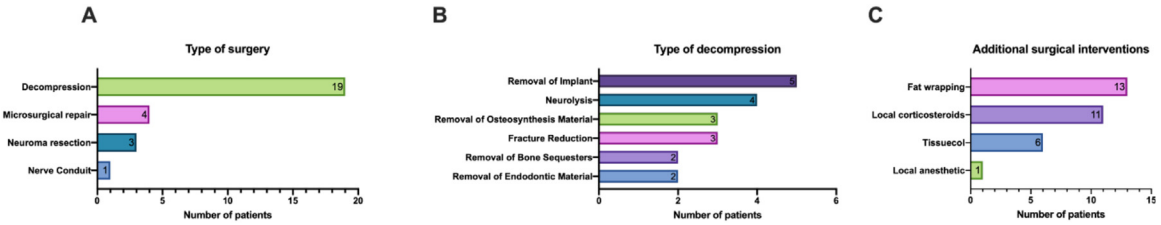


*Fig. 1.* The surgical procedures performed. (A) The types of surgical procedure. (B) Decompression was further subdivided into six categories. (C) The additional surgical interventions performed.

'no improvement') during the subgroup analysis.

The statistical significance of associations between different subgroups and improvement was assessed using Fisher's exact test. All tests were conducted at a 95% confidence interval. A *P*-value of 0.05 was considered significant. No additional statistical methods were used to control for possible confounding. The data analysis was done in Microsoft Excel 2017 (Microsoft Corp., Redmond, WA, USA) and using IBM SPSS Statistics for Macintosh, version 26.0 (IBM Corp., Armonk, NY, USA).

## Results

This retrospective study included 29 patients, 21 female (72%) and eight male (28%). Their mean age was 47 years (range 25–75 years) and 55% were younger than 50 years of age. These patients underwent a total of 30 surgical interventions at the university centre. Implant surgery was the main cause of injury ($n = 9$, 31%), followed by third molar removal ($n = 6$), facial fractures ($n = 4$), bilateral sagittal split osteotomy (BSSO) ($n = 4$), endodontic treatment ($n = 3$), and other causes ($n = 3$). Most injuries involved the third branch of the trigeminal nerve: IAN 62% ($n = 18$) and LN 17% ($n = 5$). The remaining injuries ($n = 6$, 21%) concerned the infraorbital nerve. Preoperatively, six patients (21%) reported purely neuropathic discomfort, six patients (21%) purely loss of perceptive function, and 17 patients (58%) both neuropathic discomfort and loss of perceptive function. Neuropathic pain was present in 62% of patients ($n = 18$). An overview of the study population is given in the **Supplementary Material** (Table S1).

The mean time interval between injury and surgery was 38 weeks (range 1–421 weeks). After correction for outliers, this decreased to 19 weeks. Eleven patients (38%) received surgical treatment within the first 3 months following injury. Only two patients underwent surgery after more than 1 year, with a time interval of 181 and 421 weeks, respectively; these were considered outliers in the statistical analysis.

The affected nerve was visualized during 26 interventions (87%). The remaining interventions involved the removal of osteosynthesis screws (two patients) and dental implants (two patients), this without direct visualization of the nerve. The most common intraoperative observation was nerve compression ($n = 15$), followed by partial nerve transection ($n = 10$) and fibrosis ($n = 6$). Complete nerve transection was observed in two patients, and four patients had developed a neuroma. These observations in combination with the cause of injury determined the surgical procedure performed. In accordance with the observations, nerve decompression was performed in the majority of cases ($n = 19$). This was further subdivided into dental implant removal ($n = 5$), neurolysis ($n = 4$), fracture reduction ($n = 3$), removal of osteosynthesis screws ($n = 3$), removal of endodontic material ($n = 2$), and removal of bone sequestra ($n = 2$). Other procedures were microsurgical repair ($n = 4$) and neuroma resection ($n = 3$), and one patient received a nerve conduit. In most cases, additional surgical interventions were performed. These included buccal fat nerve wrapping (BFW) ($n = 13$), local corticosteroid injection ($n = 11$), Tissucol application ($n = 6$), and local anaesthesia injection ($n = 1$). An overview of the interventions performed is given in Fig. 1.

The mean duration of follow-up was 49 months (range 2–175 months). During follow-up, 20 patients (69%) showed improvement. One patient (4%) showed complete resolution of symptoms, 12 patients (41%) improved a lot but still experienced symptoms, and seven patients (24%) showed some improvement (Fig. 2). Seven patients (35%) showed improvements in both neuropathic discomfort and loss of perceptive function symptoms. Purely loss of perceptive function improved in six patients (30%) and purely neuropathic discomfort in seven patients (35%). Nine patients (31%) showed no improvement and none got worse following surgery.

Fourteen patients specifically reported dysesthesia preoperatively. During follow-up, eight of them showed improvement in dysesthesia. Three patients reported complete resolution of the dysesthesia, although they still experienced other symptoms. Most patients with neuropathic pain showed a substantial pain improvement during follow-up (13/18, 72%) and two patients became pain-free (Fig. 3).

Subdivision by cause of injury showed that 55% of patients (5/9) with an implant surgery-related injury improved. In the group with a third molar removal-related injury, all patients (6/6) reported an improvement after surgery. Those with BSSO- and fracture-related injuries showed a 50% improvement rate (IR) (2/4 and 2/4, respectively). Patients with

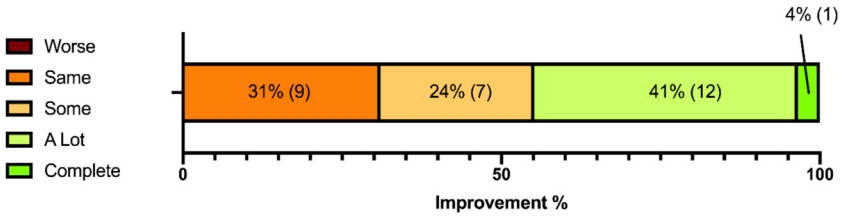


*Fig. 2.* Improvement in symptoms subdivided on an ordinal scale. Overall, 69% showed an improvement. (Worse, symptoms were worse; Same, symptoms were unchanged; Some, symptoms had improved a little; A lot, symptoms had improved greatly; Complete, complete resolution of the symptoms).

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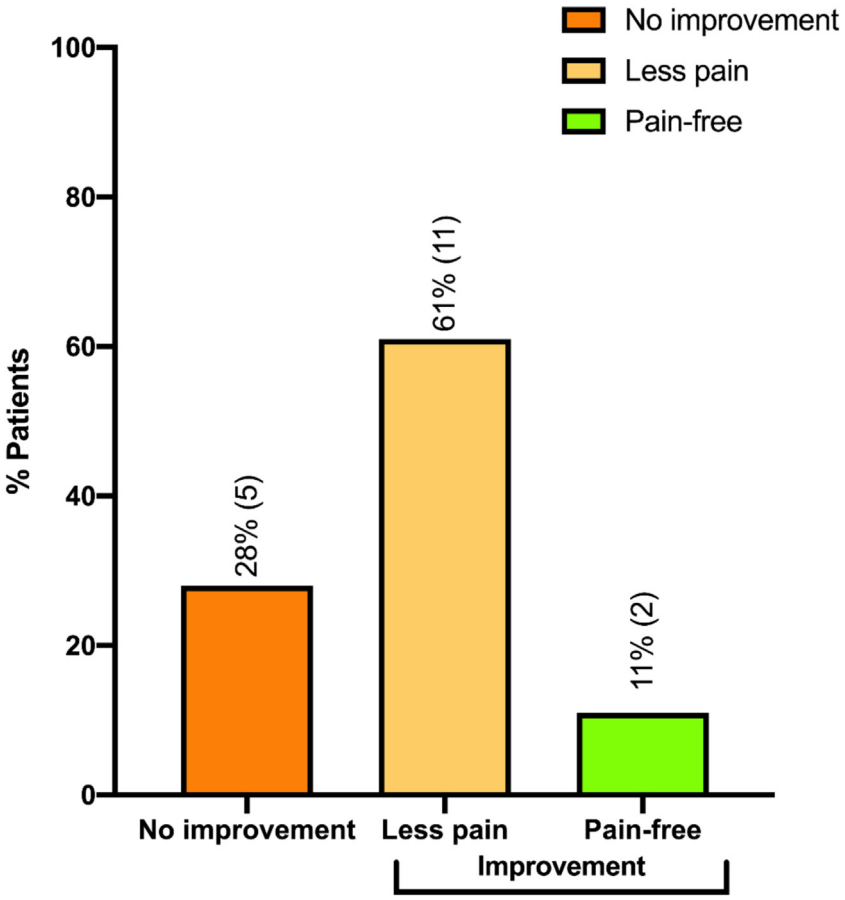


*Fig. 3*. Improvement in pain for patients diagnosed with neuropathic pain preoperatively. Improvement in pain was subdivided into no improvement, less pain, and pain-free.

an endodontic-related injury showed an IR of 67% (2/3). All patients with a nerve injury due to other causes showed an improvement (3/3). Furthermore, subdivision by type of procedure showed that 58% (11/19) improved after nerve decompression. After microsurgical nerve repair, all patients (4/4) showed an improvement. Neuroma resection resulted in an IR of 67% (2/3). One patient received a nerve conduit, but did not improve during follow-up.

Subgroup analysis showed that sex significantly affected the outcome. All male patients (8/8) showed improvement, in comparison with 57% of female patients (12/21). This association between sex and improvement was statistically significant, as assessed by Fisher's exact test ($P = 0.033$). Younger patients showed a better IR. Patients younger than 50 years showed an IR of 75% (12/16), while older patients showed an IR of 62% (8/13). This association was not significant, as assessed by Fisher's exact test ($P = 0.688$).

Different IRs were observed depending on the nerve affected. All LN injuries showed improvement (5/5), whereas IAN and infraorbital nerve injuries showed an IR of 61% (11/18) and 67% (4/6), respectively. There was no statistically significant association between the affected nerve and improvement, as assessed by Fisher's exact test ($P = 0.249$).

Surgery performed within 3 months following injury resulted in a superior IR of 73% (8/11) when compared to patients operated between 3 and 12 months following injury (IR 63%; 10/16). The association between time interval and improvement was not statistically significant, as assessed by Fisher's exact test ($P = 0.692$). Both outliers (time interval >12 months) reported some improvement during follow-up.

The diagnosis of neuropathic pain preoperatively negatively affected the outcome. When neuropathic pain was absent, 82% (9/11) showed improvement. If present, the IR was 61% (11/18). However, the association between neuropathic pain and improvement was not significant, as assessed by Fisher's exact test ($P = 0.412$). Figure 4 illustrates the effect of preoperative neuropathic pain on improvement.

One additional surgical procedure, BFW, resulted in a significantly superior IR. During this procedure, a part of the buccal fat pad is harvested and wrapped around the nerve before closure of the wound. These patients showed an IR of 92% (12/13). When the BFW procedure was not performed, the observed IR was 50% (8/16). The association between BFW and improvement was statistically significant, as assessed by Fisher's exact test ($P = 0.02$).

The investigation of medication use showed that 20 patients (69%) used pain medication preoperatively and 11 patients (38%) took more than one drug. Regarding these medications, most were typical pain medications: 18 patients were taking analgesics and nine were taking opioids. Atypical pain medications were also prescribed: five patients were using

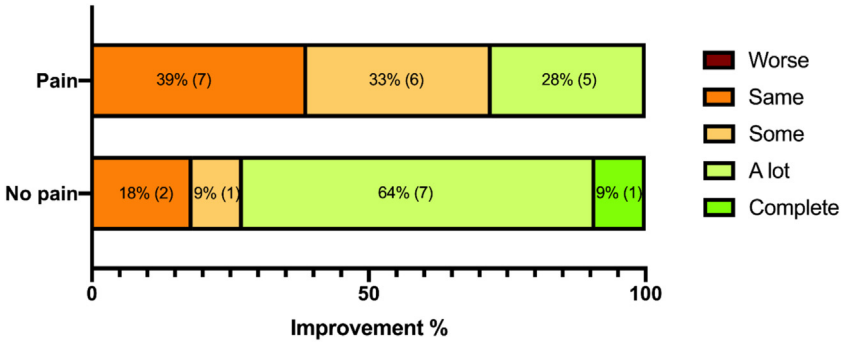


*Fig. 4*. Comparison of the improvement in symptoms between patients with preoperative neuropathic pain and patients with no preoperative pain. In both groups, the majority of patients showed an improvement (61.1% vs 81.8%). Although neuropathic pain negatively affected the outcome, the association was not significant (Fisher's exact test, $P = 0.412$). (Worse, symptoms were worse; Same, symptoms were unchanged; Some, symptoms had improved a little; A lot, symptoms had improved greatly; Complete, complete resolution of the symptoms).

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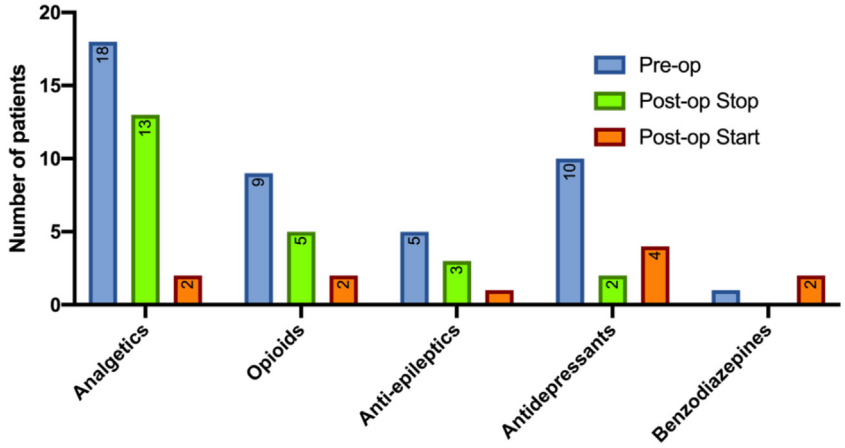


*Fig. 5*. Medication use pre- and postoperative. The drugs were divided into five categories. The numbers of patients who took the medication preoperatively and who stopped or started the medication postoperatively are shown.

anti-epileptics, 10 were using antidepressants, and one was using benzodiazepines. Medication use decreased after the surgery (Fig. 5). Thirteen patients stopped using analgesics, five stopped using opioids, three stopped using anti-epileptics, and two stopped using antidepressants. However, some patients started taking medication postoperatively. Five patients started taking analgesics, four started taking opioids, two started taking anti-epileptics, eight started taking antidepressants, and three started taking benzodiazepines. When atypical pain medication or multiple drugs were prescribed preoperatively, the chance of improvement tended to decline.

The BPI was completed by 25 patients (86%) at the last follow-up. This showed that 16 patients (64%) experienced persistent pain due to their nerve injury. Their answers were analysed further. Pain was scored on a visual analogue scale (VAS) from 0 (no pain) to 10 (worst imaginable pain). The mean pain score was 4.4. Pain scored at its worst and its best resulted in a mean score of 5.5 and 3.1, respectively. Of note, a longer interval between injury and surgery resulted in higher pain scores, and female patients scored higher than male patients. Interference with different aspects of daily life showed the substantial psychosocial burden of neuropathic pain. The BPI results for the 16 patients experiencing persistent pain are reported in Table 1.

*Table 1*. Overview of the BPI results ($n = 16$).[a]

| Question (VAS, range 0–10) | Mean | None ($n$) | Mild ($n$) | Moderate ($n$) | Severe ($n$) |
|---|---|---|---|---|---|
| Average pain | 4.4 | 1 | 8 | 5 | 2 |
| Pain at its worst | 5.6 | 0 | 4 | 9 | 3 |
| Pain at its least | 3.1 | 3 | 8 | 4 | 1 |
| Interference with general activity | 3.6 | 4 | 5 | 6 | 1 |
| Interference with mood | 4.8 | 2 | 6 | 5 | 3 |
| Interference with work | 2.1 | 10 | 1 | 4 | 1 |
| Interference with relationships | 2.8 | 6 | 6 | 2 | 2 |
| Interference with sleep | 3.8 | 3 | 7 | 4 | 2 |
| Interference with enjoyment | 4.6 | 3 | 5 | 4 | 4 |

BPI, Brief Pain Inventory (Short Form) questionnaire; VAS, visual analogue scale.

[a] This table shows the BPI results of the 16 patients who reported persistent pain at last follow-up. Pain and interference were scored on a VAS scale from 0 (no pain/interference) to 10 (worst imaginable pain/complete interference). The mean scores are shown. Furthermore, the VAS scores were divided in groups according to severity: none (VAS 0), mild (VAS 1–4), moderate (VAS 5–7), and severe (VAS 8–10). The number of patients per group are shown for each question.

## Discussion

This study showed that surgical treatment for PTTN successfully reduced neuropathic symptoms. During follow-up, pain symptoms improved and medication use decreased.

The main indication for surgical intervention was a lack of improvement or a progression of symptoms, combined with a suspected nerve lesion or compression. This is in line with the indications established by Zuniga and LaBanc in 1993 and a recent algorithm for the management of PTTN developed by Renton and der Cruyssen[13,15]. The definitive surgical approach depended on the mechanism of injury and intraoperative observations. Also, radiological imaging was used to evaluate the injury (e.g., cone beam computed tomography and magnetic resonance neurography).

The majority of patients reported improvement after the surgical intervention. However, only one patient reported complete resolution of the symptoms. Spontaneous recovery may occur during follow-up, and this could have influenced the surgical outcome. Functional recovery can take up to 1 year to complete. The mean duration of follow-up was 49 months (range 2–175 months). At the time of the study, two patients had a follow-up time of less than 1 year (respectively 2 and 8 months). As both patients already showed an evident improvement, they were included in the study. Nevertheless, the further evolution of their recovery is missing.

Subgroup analysis was limited due to the small study population. Differences in IR should therefore be seen as trends and these need further investigation in larger studies. Still, some differences are in accordance with those reported previously in the literature. Bagheri et al.[16,17] showed comparable overall IRs. They showed that LN repair had the best IR and that increasing patient age negatively affected the outcome. Preoperative pain, the cause of injury, intraoperative observations, and type of surgery did not significantly affect the outcome[17]. Neuropathic pain is a challenging symptom to tackle and is therefore sometimes seen as a relative contraindication to surgery[18]. The analysis showed that 13 patients (72%) had an improvement in their pain after surgery and two patients became pain-free. However, 16 patients (64%) reported persistent or returned pain at the last follow-up. Previous studies have recommended a 12-month follow-up after surgery to evaluate pain recurrence and the associated pain level[19,20].

The correct timing for trigeminal nerve repair continues to be a controversial subject. Most studies recommend nerve repair 3 months after injury to obtain successful neurosensory recovery before chronic neuropathic pain develops[19,21]. However, during the first 3 to 6 months, a conservative 'watch and wait' policy is often the first choice, since spontaneous recovery can occur[10,11]. This approach results in a

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time delay concerning surgical treatment. At 12 months after surgery, a significant drop in the chance of improvement occurs[17]. This could be due to Wallerian degeneration and the formation of scar tissue. The mean time interval in this study was 19 weeks (without outliers) and thus beyond the prioritized time interval of 3 months. Nevertheless, an overall IR of 69% was observed. Subgroup analysis showed a superior IR when treatment occurred within 3 months. Also, a longer time interval resulted in higher pain scores on the BPI. However, the difference was modest and not significant. Two patients were treated more than 12 months after injury; both showed some improvement. This could be the result of the placebo effect, since both reported high pain scores at the last follow-up.

In contrast to much of the previous literature, symptoms in this study were differentiated into neuropathic discomfort and loss of perceptive function (e.g., neurosensory deficits). In the statistical analysis, each symptom was seen as equal. However, in daily practice, neuropathic pain and dysesthesia have a far greater impact on patient QoL. An improvement on qualitative sensory testing should not be seen as a surgical success if the patient is still suffering from other debilitating symptoms. Therefore, standard follow-up and clinical research should include patient-reported outcomes and questionnaires evaluating QoL.

The BFW procedure resulted in a significantly higher IR. This procedure has been shown to be a promising new strategy in LN and IAN repair. In other disciplines, the use of autologous fat grafting in peripheral nerve repair is already known to be successful[22]. As shown in molecular research, adipose-derived stem cells could be the key to this success[23–25]. In the specialty of oral and maxillofacial surgery, the buccal fat pad is well known, easy accessible, and lends itself perfectly for use as an autologous fat graft. More evidence regarding this new technique should be obtained through future research.

Medication use, especially analgesics and opioids, decreased postoperatively. This might indicate the success of the surgical intervention. Pharmacological treatment for trigeminal neuropathy is challenging. It is difficult to obtain a complete response and intolerance often occurs[1,12]. Eventually, patients become dependent on their medication and medication with a central working mechanism is needed. This could explain why only a few patients ceased their atypical pain medication postoperatively and some started taking them.

Finally, neuropathic symptoms are known to have a serious impact on the patient's life and interfere with daily activities, as was well illustrated by the BPI results. Treatment should not be restricted to medication and surgery alone. PTTN requires a holistic approach with attention to psychological wellbeing. Cognitive behavioural therapy has already been shown to be a useful asset[1].

The main limitations of this study are associated with its retrospective nature. Consultations and patient reports, preoperatively and during follow-up, were not standardized. Improvement was reported, taking into account both objective (e.g., qualitative sensory testing) and patient-reported outcomes. The objective assessments were not specified separately. This study included a heterogeneity of causes and various surgical interventions to produce an appropriate study population size. Therefore, the results are rather non-specific for cause or intervention. As there was no preoperative BPI, the results could not be correlated with the surgical outcome. Nevertheless, the BPI added value in follow-up and the interpretation of long-term improvement.

As this study showed promising results, surgical intervention should be considered an option in the treatment of PTTN, especially when signs of spontaneous recovery remain absent in the first 3 months following injury. Future prospective research with large study populations is needed to further establish the role and timing of surgery, its indications, and the effect of different variables on the outcome. Future research should follow standardized pre- and postoperative protocols, including the following: a minimum follow-up of 1 year, regular time intervals, qualitative and quantitative sensory testing, and pre- and postoperative BPI questionnaires.

## Funding

No grants were used to support this study.

## Competing interests

The authors declare no conflict of interest, financial, personal, or otherwise.

## Ethical approval

Ethical approval was obtained from the Ethics Committee of the University Hospital Leuven (reference number S62333).

## Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.ijom.2020.05.004.

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