Prediction of Postoperative Pain After Mandibular Third Molar Surgery

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Aims: *To evaluate the predictive potential of preoperative psychological and psychophysiological variables in estimating severity of postoperative pain following mandibular third molar surgery (MTMS).* ***Methods:*** *Following ethical committee approval and informed consent, 40 consecutive patients scheduled for MTMS were included. Preoperative psychometric indicators of anxiety, depression, and vulnerability were evaluated by patient questionnaires. Thermal thresholds and heat pain perception (1 second phasic stimuli: 44°C to 48°C) were evaluated with quantitative sensory testing techniques. Standardized surgery was performed during local anesthesia. Postoperative pain management was with rescue paracetamol and ibuprofen. The patients were instructed to record each day their pain at rest and during dynamic conditions, and their requirement of analgesics for 14 days following surgery.* ***Results:*** *Thirty-eight patients completed the study. Eight patients were readmitted because of pain. During the postoperative period, one or more episodes of moderate to severe pain (> 30 on a visual analog scale) was reported by 60% (23/38) at rest, 63% (24/38) during mouth-opening, and 73% (28/38) during eating. In a multiple regression model, the combination of psychological vulnerability and heat pain perception rendered a predictive model that could account for 15 to 30% of the variance in postoperative pain during resting and dynamic conditions (*P = .03 to .001).***Conclusion:** *Implementation of clinically relevant preoperative screening methods may offer more efficacious postoperative pain therapies to pain-susceptible individuals undergoing mandibular third molar surgery.* **J OROFAC PAIN 2010;24:189–196**

Key words: mandibular third molar surgery, pain measurement/methods, pain postoperative, predictive value of tests, quantitative sensory testing

Surgical removal of impacted mandibular third molars is one of the most common procedures in oral surgery with 20,000 to 25,000 procedures performed each year at Swedish oral and maxillofacial surgical clinics.[1] Severe acute pain following mandibular third molar surgery has been reported in 16 to 20% of the patients.[2,3] Removal of mandibular third molars may significantly affect patients' quality of life, particularly during the first 3 postoperative days.[4] Only 2% of the patients have been reported to be able to maintain their ordinary food intake in this period and significant eating difficulties may continue for up to 4 days after surgery.[4]

Table 1 Psychological Vulnerability

Do your hands often shake or tremble?
Is your appetite always poor?
Do you suffer badly from frequent severe headaches?
Do you usually have great difficulty in falling asleep or staying asleep?
Do you often suddenly become frightened?
Do you often get spells of complete exhaustion or fatigue?
Do you often take tranquillizers or sleeping pills?
Do you often feel pain in different places, such as your stomach or your back or your chest?
Do you suffer from nervous disorder?
Do you often have spells of severe dizziness?
Do sudden noises make you jump or shake badly?
Do you usually feel unhappy and depressed?
Does your work fall to pieces when the boss or a superior is watching you?
Does you heart often race like mad for no good reason?
Do you frequently feel faint?
Do you have difficulty making friends?
Does it make you angry to have anyone tell you what to do?
Do you prefer to keep to yourself?
Does every little thing get on your nerves and wear you out?
Do frightening thoughts keep coming back in your mind?
Are your extremely shy or sensitive?
Do people usually misunderstand you?

Psychological vulnerability was scored by counting the number of affirmative answers from 12 selected items merged with 10 indifferent items. The 12 selected items above are shown in italics.

Despite the increased awareness of the importance of effective pain management following surgical procedures, inadequate postoperative pain relief still poses a significant clinical problem.[5] Postoperative pain studies demonstrate a considerable individual variation in perception of pain, and in the physical and psychological distress evoked by the pain. In order to identify patients at particular risk of developing severe discomfort and pain, a number of preoperative screening methods have been developed that may lead to more efficient pain management strategies.[6] Previous studies have indicated that preoperative pain,[6–10] patient's expectations,[6] gender,[9] age,[7,9,11] anxiety,[6,7,9,12–14] depression,[7,12] psychological vulnerability,[8,11] catastrophizing behavior,[13] and preoperative responses to experimental pain stimuli[6,10,11,14–17] are significantly correlated with the severity of postoperative pain. However, in most studies the statistical correlation between preoperative indicators and postoperative pain ratings has been relatively weak.

The objective of the present study was to evaluate the predictive potential of preoperative psychological and psychophysiological variables in estimating severity of postoperative pain following mandibular third molar surgery. To the authors' knowledge, this study is the first to examine preoperative prediction of the severity of oral surgery-related postoperative pain.

Materials and Methods

The Ethics Committee at Lund University Hospital approved the study protocol. Patients scheduled for outpatient mandibular third molar surgery, at the Department of Oral and Maxillofacial Surgery, Malmö University Hospital, were considered eligible for the study. Exclusion criteria were: age < 18 years, impaired communicative or cognitive abilities, diagnosed neurological disease, diagnosed diabetes mellitus, medication with opioids, and contraindications to use of nonsteroidal anti-inflammatory drugs (NSAIDs).

Patients

Between August and December 2005, 40 consecutive patients were included in the study. Two patients did not return their diaries in spite of repeated requests by phone and mail, and were therefore excluded from the study. Thus 38 patients (15 men and 23 women [age 29.5 (25.2 to 37.7) years]) completed the study. The indications for surgery were pericoronitis, caries, and periapical lesions.

Preoperative Evaluation

The patients were preoperatively informed about the study by phone. On the day of surgery, 1 to 2 hours before the surgical procedure, the patients were verbally and in writing informed about details of the study and thereafter signed a written consent. Psychometric indicators of anxiety and depression were evaluated by patient questionnaires: the Hospital Anxiety and Depression Scale (HADS), State-Trait Anxiety Inventory (STAI-S [state] and STAI-T [trait])[18] and psychological vulnerability was evaluated by a test validated for surgical procedures (Table 1).[8,11] The validated Swedish version of the short-form McGill Pain Questionnaire (SF-MPQ)[19] was used for evaluation of preoperative pain by the use of Present Pain Index (PPI, 0 to 5) and a visual analog scale (VAS, 0 to 100 mm [0 = no pain, 100 = the worst pain imaginable]).

Quantitative sensory testing (QST) was performed with a Modular Sensory Analyzer ([MSA], Somedic AB) by using a 25 × 50 mm^2 contact thermode applied to the skin. When the patients had been familiarized with the QST procedure, assessments were made with the thermode applied

to the medial side of the nondominant calf. Baseline temperature was adjusted to 32°C, and warm detection threshold (WDT) and heat pain threshold (HPT) were assessed with a ramp rate of 1°C/s. The patients were asked to immediately activate a button when the stimulus was perceived either as warm (WDT) or painful (HPT), respectively. Heat pain perception was evaluated by five double-blinded, randomized stimuli of 1 second duration, at 44, 45, 46, 47, and 48°C, respectively, with an interstimulus interval of 60 seconds. The patients were asked to indicate the level of pain on a 100 mm VAS ruler immediately after each stimulus. For heat pain perception, two parameters were used: summation of VAS scores during application of the five stimuli 44 to 48°C, and VAS scores at 48°C.

Analgesia

Following QST assessments, paracetamol (2 g orally) was given 1 hour prior to surgery. For local anesthesia, 3.6 mL lidocaine 20 mg/mL with epinephrine 12.5 μg/mL (Xylocain Epinephrine, AstraZeneca) was used as a block of the inferior alveolar, buccal, and lingual nerves. The patients were discharged from the hospital directly after the surgery and were informed to use rescue doses orally of paracetamol (1 g; maximum daily dose 4 g), supplemented by ibuprofen (600 mg; maximum daily dose 1,800 mg). Analgesic requirements were registered by the patients in a standardized diary (see below).

Surgical Procedure

All procedures were performed by the same surgeon (LE). The duration of surgery was defined as time from the start of the surgery until the last suture. The angular positions of the mandibular third molars were vertical (n = 11), mesioangular (n = 17), horizontal (n = 5), and distoangular (n = 5). For exposure of partially erupted or nonerupted teeth (n = 35), a gingival incision was made from the buccal surface of the first molar to the anterior part of the mandibular ramus. A mucoperiostal flap was raised and covering bone, if any, was removed with a burr. If necessary the tooth was separated and removed by the aid of an elevator. Finally, the wound was thoroughly cleansed with irrigation and debrided with a curette and closed with simple interrupted sutures (Vicryl 4-0 [Ethicon]). Totally erupted teeth (n = 3) were removed by the aid of an elevator/forceps and as needed separated as mentioned above for partially erupted teeth. The overall difficulty of the extraction process was rated by the surgeon on a numerical rating scale (NRS), 0 to 10 [0 = very easy, 10 = very difficult].

Postoperative Evaluation

The patients were instructed to record daily pain assessments and requirement of analgesics in the standardized diary. Intensity of pain was indicated by VAS at rest, during opening of the mouth, during drinking, and during eating. Orofacial postsurgical pain was evaluated in the evening on the day of surgery (day 0) and then twice (in the morning and in the evening) on the following days up to and including postoperative day 14 (day 14). Maximal VAS was defined as the highest reported postoperative VAS score. Moderate pain was defined as VAS scores above 30 mm[20] and severe pain as VAS scores above 70 mm.[21]

The patients were instructed to contact the attending surgeon in case of a suspected postoperative complication. All patients were followed up by phone calls postoperatively on day 1, day 4, and day 10. At day 14, the patients evaluated postoperative pain by a second SF-MPQ. The patients' diaries were returned by regular mail.

Data Analyses

First, the univariate association between potential preoperative predictors and postoperative pain was estimated by the Pearson's correlation coefficient (*r* [SPSS 11.5]) and the variable "gender" was estimated by contingency coefficients. The questionnaire scores were compared by the Mann-Whitney test. Postoperative VAS ratings for Days 0 to 14 were summed up in order to minimize the likelihood of mass significance.[22] Second, the variables were tested in a multiple regression model using a forward stepwise method calculating the multiple correlation coefficient *(R)*. Predictors with *P* values ≤ .05 were entered in the analyses. To be retained in the model, a $P \leq .1$ in the model was required. Collinearity was tested by variance inflation factors (VIF) and variables were excluded if VIF was ≥ 2 (SPSS 11.5). The number of predictors included in a multivariate model should not exceed 10% of the number of participants in the study,[22] a criterion that was fulfilled in the study since the tested variables in the multiple regression analysis were heat pain perception, psychological vulnerability and anxiety scores (HADS-anxiety and STAI-T), and the number of patients was 38. Data are presented as median (25 to 75%, interquartile range), unless otherwise indicated. A $P < .05$ was considered statistically significant.

Table 2 Preoperative Assessments

Preoperative variables	Median (interquartile range)
PPI (0 to 5)	0 (0–0)
Preop pain VAS (0 to 100)	0 (0–0)
HADS-anxiety (0 to 21)	5 (2–7)
HADS-depression (0 to 21)	1 (0–3)
STAI-S (20 to 80)	34 (27–44)
STAI-T (20 to 80)	31 (26–41)
Psychological vulnerability test (0 to 12)	1 (0–2)
WDT (°C)	36.4 (35.2–37.0)
HPT (°C)	45.2 (43.5–46.8)
Heat (48°) pain perception VAS (1 to 100)	59 (32–85)
Summed heat (44°–48°) pain perception VAS (1 to 100)	139 (53–230)

Results

Preoperative Evaluation

Pain before surgery assessed by patient PPI and VAS was reported by 6/38 patients (Table 2). The pain locations were the knee and foot (n = 1), the neck and arm (n = 1), the neck and shoulders (n = 2), the wrist (n = 1), and the jaw (n = 1). Four of these patients reported preoperative VAS scores ≤ 15, one patient reported VAS = 35, and one patient reported a VAS score = 50. None of the patients were in continuous treatment with analgesics.

Surgical Procedure

Average duration of surgery was 11 (range 2 to 21) minutes and overall difficulty of the extraction process was rated by the surgeon as an average of 6 (NRS, range 2 to 10).

Complications

Eight patients were readmitted to the clinic because of pain 4 to 9 days postoperatively. Partially or completely dislodged blood clots in the tooth sockets were observed in all cases, and the condition was diagnosed as alveolitis. Treatment consisted of gentle irrigation with 0.9% saline and insertion of a gauze with oxytetracycline hydrochloride and polymyxin B paste (Terracortril with polymyxin B [Pfizer AB]), used for 2 days. Six of the patients had one postoperative visit and two had two visits.

These patients with postoperative complications scored significantly higher compared to the patients without postoperative complications for HADS anxiety, (average scores 8 [6 to 10] and 3 [1 to 7], respectively, $P = .004$) and STAI-T (average scores 38 [32 to 47] and 28 [25 to 40], respectively, $P = .04$)

Postoperative Analgesia

The total doses of paracetamol and ibuprofen administered by the patients during the 14 postoperative days averaged 13.5 (6.5 to 22.2) g and 7 (3.9 to 13.8) g, respectively.

Postoperative Pain Assessments

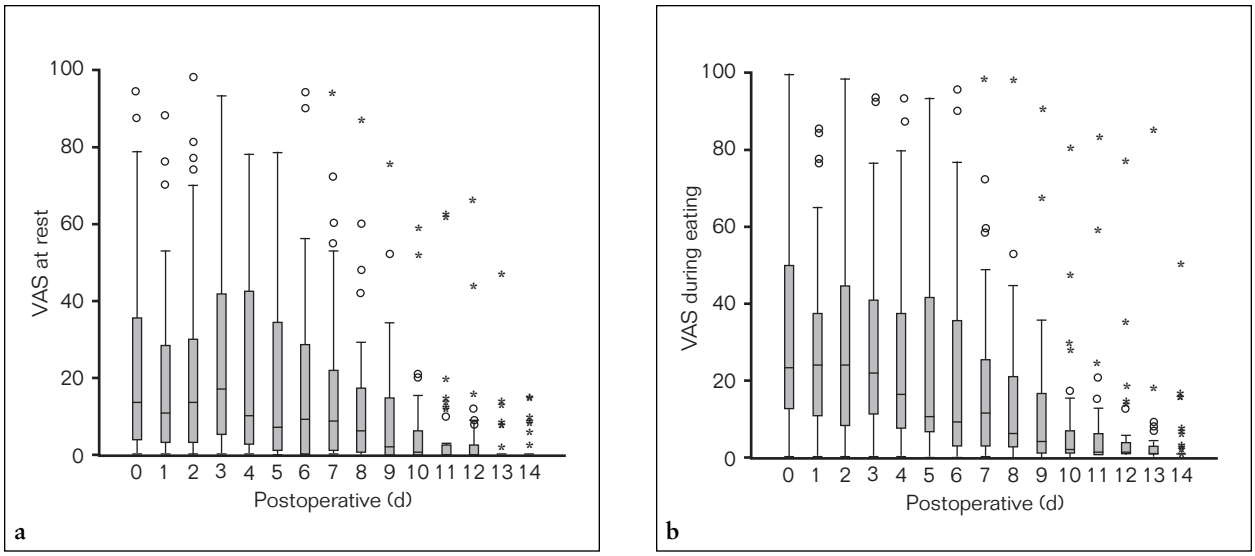
The highest VAS score was reported during eating. Pain scores at rest and during eating for Days 0 to 14 are illustrated in Figs 1a and 1b. During the postoperative period, one or more episodes of moderate to severe pain was reported by 60% (23/38) at rest, 63% (24/38) during opening of the mouth, 60% (23/38) during drinking, and 73% (28/38) during eating, respectively. Severe pain was reported by 24% (9/38) at rest, 26% (10/38) during opening of the mouth, 26% (10/38) during drinking, and 32% (12/38) during eating.

Prediction

In the *univariate analyses,* preoperative heat pain perception at 48°C, psychological vulnerability and anxiety scores (STAI-T and HADS-anxiety) were significantly correlated to postoperative pain (Table 3). No significant correlation was found between age, gender, summed (44 to 48°C) heat pain perception, preoperative pain, HADS-depression, STAI-S, surgical time or surgical difficulty, and postoperative pain (VAS).

The paracetamol requirement did not correlate with the preoperative variables ($P > .1$), whereas the ibuprofen requirement significantly correlated with STAI-T ($r = 0.32$, $P < .05$) and HADS-anxiety ($r = 0.41$, $P = .01$).

In the *multiple regression model,* psychological vulnerability was a significant predictive variable in all models using the sum of reported postoperative pain for days 0 to 14 ($P < .01$), whereas heat (48°C) pain perception was a significant predictor in all models using maximum reported pain for days 0 to 14 ($P < .05$) (Table 4). In a subgroup analysis, when patients with postoperative complications were excluded, psychological vulnerability was a significant predictor for the sum of reported postoperative pain at rest, days 0 to 14 during



Figs 1a and b Box plots (median, interquartile range) representing pain assessments by VAS scores at postoperative days 0 to 14 *(a)* at rest and *(b)* during eating. The whiskers represent largest observed values within 1.5 box-lengths from upper to lower border of the box; ° = outliers; * = extreme outliers.

Table 3 Univariate Analyses

	Postoperative pain at rest days 0 to 14		Postoperative pain during mouth opening days 0 to 14		Postoperative pain during drinking days 0 to 14		Postoperative pain during eating days 0 to 14	
	Sum	Max	Sum	Max	Sum	Max	Sum	Max
Age	–0.094	–0.249	–0.086	–0.258	–0.065	–0.175	–0.104	–0.288
Gender**	0.972	0.662	0.697	0.686	0.697	0.657	0.707	0.662
Preoperative pain VAS	–0.192	–0.285	–0.188	–0.306	–0.151	–0.193	–0.187	–0.296
HADS anxiety	**0.418****	0.302	**0.376****	0.249	**0.331***	0.139	**0.421****	0.207
HADS depression	0.168	0.136	0.174	0.139	0.172	0.103	0.157	0.088
Psychological vulnerability	**0.536*****	**0.360***	**0.470****	0.245	**0.463****	0.229	**0.448****	0.215
STAI-S	0.084	–0.052	0.042	–0.084	0.031	–0.142	0.043	–0.168
STAI-T	**0.378***	0.242	**0.339***	0.126	0.316	0.098	**0.392***	0.116
Warm detection threshold	–0.012	–0.165	–0.144	–0.274	–0.154	–0.241	–0.144	–0.243
Heat pain threshold	–0.079	–0.132	–0.156	–0.231	–0.141	–0.264	–0.168	–0.235
Heat (48°C) pain perception	0.256	**0.364***	0.246	**0.343***	0.298	**0.442****	0.273	**0.432****
Summed heat (44 to 48°C) pain perception	0.184	0.272	0.186	0.265	0.196	**0.347***	0.205	0.237
Surgery time	0.130	0.035	0.177	0.032	0.122	0.026	0.159	0.052

Univariate analysis of correlation (indicated as Pearson s correlation coefficient *[r]*, gender indicated as contingency coefficients) between preoperative predictors (vertical row) and summed postoperative (horizontal row [VAS values]. Significant correlations are in bold. *$P < .05$, **$P < .01$, ***$P < .001$.

mouth opening and during drinking (R = 0.37 – 0.44). HADS anxiety was a significant predictor for sum of reported postoperative pain for days 0 to 14 during eating (R = 0.42). In the subgroup analysis, heat (48°C) pain perception was a significant predictor for maximum reported pain during drinking (R = 0.42) and during eating (R = 0.39). Multiple regression analyses enabled calculation of prediction models that accounted for 15 to 30% (R^2) of the total variance in postoperative dynamic pain ratings during standardized and clinically relevant conditions.

Discussion

The present study examined the correlation between preoperative variables (measures of anxiety, psychological vulnerability, pain, and response to painful heat stimuli) and postoperative pain. The results suggest that patients with a high risk of experiencing severe postoperative pain may be identified prior to the surgery. Such stratification of patients may be important not only in allocating treatment resources, but also in identifying relevant groups of individuals to be included in trials of new analgesics.[16] Surgical

Table 4 Stepwise Multiple Regression Analyses of Preoperative and Summed Measures of Postoperative Pain (VAS) at Rest, During Mouth Opening, During Drinking, and During Eating

VAS (days 0 to 14)	*R*	R^2	Adjusted R^2	F	b	SE	β	*t*
At rest								
Sum	0.54	0.29	0.27	14.49**				
Max	0.36	0.13	0.11	5.51**				
Predictors								
Psychological vulnerability					168.99	44.39	0.54	3.81**
Heat (48°) pain perception					0.36	0.15	0.36	2.35*
During opening the mouth								
Sum	0.47	0.22	0.20	10.20**				
Max	0.34	0.12	0.09	4.79*				
Predictors								
Psychological vulnerability					151.45	47.41	0.47	3.19**
Heat (48°) pain perception					0.32	0.15	0.34	2.19*
During drinking								
Sum	0.46	0.21	0.19	9.82**				
Max	0.44	0.20	0.17	8.72**				
Predictors								
Psychological vulnerability					142.62	45.51	0.46	3.13**
Heat (48°) pain perception					0.42	0.14	0.44	2.96**
During eating								
Sum	0.45	0.20	0.18	9.05**				
Max	0.43	0.19	0.16	8.26**				
Predictors								
Psychological vulnerability					157.28	52.28	0.45	3.01**
Heat (48°) pain perception					0.41	0.14	0.43	2.87**

F = F statistic; b = regression coefficient; SE = standard error; β = standardized regression coefficient; *t* = *t* statistic. *$P < .05$; **$P < .01$.

removal of third mandibular molars has been considered an appropriate inflammatory pain model for testing of efficacy of analgesics.[23]

Preoperative Sensory Testing

While a number of studies have investigated the correlation between preoperative responses to experimental pain stimuli and clinical postoperative pain,[10,11,16,17] this is, to the authors knowledge, the first study to examine an oral surgical procedure. The findings are generally in good agreement with previous studies although a heterogeneity in regard to stimulation methods, assessment methods, and surgical procedures seems to exist. Preoperative pain tests may predict 5 to 43% of the variance in postoperative experience, depending on the testing paradigm used. Most of the testing methods are elaborate although simple patient-controlled electrical devices have been used for bedside tests.[17,24]

Anxiety

Most individuals experience some degree of apprehension or anxiety when attending a dentist for treatment. In a recently published study investigating 67 anxiety-provoking stimuli present in the dental setting, surgery was the highest ranked and 22% rated dental surgery as extremely anxiety-provoking.[25] In the present univariate model, anxiety (related to trait [STAI-T] and HADS anxiety) was correlated with postoperative pain, whereas in the multiple regression model anxiety was not a predictor for postoperative pain.

Psychological Vulnerability

Psychological vulnerability, previously termed neuroticism, is defined as an inherent tendency to experience negative emotions such as anger, anxiety, guilt, and depression, with an increased susceptibility to emotional injury.[26] The present study corroborates recent findings in a laparoscopic procedure[10] where a significant correlation between psychological vulnerability and postoperative dynamic pain assessments was observed. These findings are also in agreement with a large study[11] which reported that preoperative sensory testing and preoperative psychological vulnerability were independent risk factors for postoperative pain after laparoscopic cholecystectomy. Cognitive vulnerability with an increased expression of uncontrollability, unpredictability, and dangerousness has been linked to dental fear.[27]

Surgical Factors

In a recent study,[28] there was no correlation between duration of surgery, extraction difficulty, and postoperative pain which is in agreement with the present study. However, a duration of the surgical procedure of more than 30 minutes has been associated with a prolonged postoperative recovery in other studies.[29,30]

Mandibular third molar surgery is a high volume procedure that is often performed on an outpatient basis. It is therefore of interest that following discharge, 73% (28/38) of patients experienced one or more episodes of moderate to severe pain and 32% (12/38) experienced severe pain during eating, which was the testing condition associated with the most intense pain. Postoperative pain assessments include pain ratings, pain-relief ratings, and requirement characteristics of analgesics (dose, time). In the present study, the analgesics were patient-controlled, but interestingly no correlation was found between experienced pain and analgesic requirement.[31] Dental pain is predominantly considered an inflammatory pain, and the analgesic efficacy for paracetamol and NSAIDs are higher for dental surgery compared to other surgical procedures.[23]

Advantages and Limitations

In most predictive studies, single factor analyses have been used and thus the multidimensional aspects of pain experience may have been overlooked.[10] The present study evaluated a combination of preoperative psychological and physiological variables. Furthermore, the follow-up period was considerably longer than in many other prediction studies. Although dental surgery is considered a minor surgical procedure, a large number of patients experienced pain episodes of moderate to severe intensity.

A limitation of the present study was that a number of univariate correlation analyses were made which may increase the risk of type I error. The study did not adjust for multiple comparisons since the correlation analyses were used to select variables to be included in the multiple regression models. In each analysis, variables were sequentially removed if the *P* value exceeded .10, which is considered a rather conservative significance level compared to other studies.[7,9] Although the relationship between the number of included predictors and the sample size follows recommended statistical guidelines,[22] the possibility of a type II error cannot be excluded due to the relatively small number of patients included in the study. On the other hand, care was taken to limit overall variance in testing conditions by studying a homogenous patient population, by using preoperative data sampling by two investigators, by standardizing the surgical procedure by one surgeon, and by regular contact with the patient during the postoperative pain assessment period. Postoperative pain assessment was made during standardized resting and dynamic conditions in order to give a clinically relevant and reliable estimate of pain.

Eight patients developed alveolitis which typically results in substantial pain. All patients were included in the models and patients with alveolitis were not accounted for separately in the statistical analysis for two reasons. First, the power of the study was calculated *a priori* and based on the numbers of the factors included in the multivariate analysis. Thus, subgroups analysis should only be made with great caution, since the necessary statistical power may be inadequate. Second, the complications were classified as alveolitis in all eight patients. These patients with postoperative complications scored significantly higher in HADS anxiety and STAI-T preoperatively, compared to the patients without postoperative complications. A higher degree of anxiety, in particular trait anxiety, may have been a contributing factor for readmission. The authors did however perform the subgroup analysis only including patients without complications and the results were almost identical to the analysis of the group as a whole.

Severe pain in the immediate postoperative period is a risk factor for development of persisting pain.[32] Even though the risk of persistent pain following lower mandibular third molar surgery is extremely low,[33,34] a high volume procedure may be associated with a relatively high absolute number of individuals who will develop persistent pain. In a study investigating 1,500 patients 5 years after third molar surgery, 2.2% experienced long-term symptoms including neuropathic pain (≤ 0.38%) that could be related to the procedure.[34]

In summary, the present study has revealed that a high number of individuals experienced episodes of moderate to severe pain following mandibular third molar surgery. Preoperative screening with a combination of psychological and psycho-physiological variables rendered a predictive model that could account for 15% to 30% of the variance in postoperative pain during resting and dynamic conditions. These findings may facilitate more aggressive pain therapies targeted at individuals at a high risk of experiencing severe postoperative pain.

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