Predictive Model for Pain Recurrence After Posterior Fossa Surgery for Trigeminal Neuralgia

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Background: Surgical exploration of the posterior fossa is the definitive treatment for trigeminal neuralgia refractory to medication, but predictors of its success in effecting long-term pain relief have not been established.

Objective: To develop a model that allows stratification of patients’ risk of postoperative recurrence of pain based on pretreatment factors.

Methods: We reviewed the records of 420 consecutive patients who underwent posterior fossa exploration by one of us (C.B.W.) for the treatment of idiopathic trigeminal neuralgia. The primary outcome measure was recurrence of trigeminal pain. The predictive value of preoperative and intraoperative factors was evaluated. Multivariate analysis revealed the statistically significant predictors of pain recurrence, permitting creation of a risk model for recurrence of pain.

Results: After surgery, trigeminal pain had lessened in 98% of patients and completely resolved in 87%. There were no perioperative deaths. After a mean follow-up of 56.3 months, 93% of patients reported significant pain improvement and 72% continued to have no pain. The estimated likelihood of pain recurrence at 8 years was 34%. Significant predictors of eventual recurrence of pain were age younger than 53 years at the time of surgery, symptoms lasting longer than 11 1/2 years, female sex, and pain on the left side in men. These factors were weighted and incorporated into a risk model that revealed 4-year pain-free survival of 89%±4% for the low-risk group, 80%±4% for the moderate-risk group, and 58%±6% for the high-risk group (data are mean±SD).

Conclusions: We developed a predictive model that stratifies the risk for eventual recurrence of pain after posterior fossa exploration for trigeminal neuralgia. This information may be useful in counseling patients regarding treatment.

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TRIGEMINAL NEURALGIA is one of the most common causes of facial pain. It is characterized by transient episodes of lancinating pain in the trigeminal distribution, often precipitated by mild mechanical irritation from activities such as brushing the teeth or chewing. Although the pathogenesis is controversial, there are effective treatments. Once medical treatments fail, surgical intervention may be advocated.13 Percutaneous lesions of the trigeminal nerve or ganglion, exploration of the posterior fossa for microvascular decompression (MVD), partial sensory rhizotomy (PSR) at the nerve root entry zone, and, more recently, stereotactic radiosurgery have been shown to ameliorate symptoms.14-47

Among the surgical treatments, posterior fossa exploration is often the preferred initial treatment, because it affords the highest success rate with the lowest complication rate.19-21,37 Several studies6,23,25,48,49 have assessed factors that predict pain relief after posterior fossa exploration for trigeminal neuralgia. A short duration of symptoms, absence of prior destructive procedures, male sex, and arterial compression of the nerve root entry zone, either individually or in combination, are predictive of long-term pain relief. Still, there is no consensus about predictors among the various studies, and there is no model that incorporates predictors to stratify the risk of postoperative recurrence based on pretreatment patient characteristics.

We performed this retrospective study to determine predictors of pain relief after posterior fossa exploration and to create a model for predicting the risk of pain recurrence.

RESULTS

During the study, 648 posterior fossa explorations for trigeminal neuralgia were per-
PATIENTS AND METHODS

PATIENTS

All patients who consecutively underwent posterior fossa exploration (n=420) for the treatment of idiopathic trigeminal neuralgia by one of us (C.B.W.) at our institution between June 1969 and September 1998 were eligible for inclusion in the study. Patients who had multiple sclerosis, a posterior fossa lesion (eg, tumor, aneurysm, or vascular malformation), or prior posterior fossa exploration were excluded. Prior percutaneous procedures for the treatment of trigeminal neuralgia were allowed.

All procedures were performed by using techniques described elsewhere. Based on operative findings, patients were treated by MVD, PSR, or both. Microvascular decompression was performed when nerve root distortion resulted from external vascular compression. Veins were coagulated and divided, whereas arteries were dissected away from the nerve and displaced with a Teflon sponge. In patients without vascular contact, a PSR was performed. A combination of MVD and PSR was performed in patients with vascular contact but without deformity of the nerve root.

DATA COLLECTION

After obtaining approval from The University of California, San Francisco, Committee on Human Research, we reviewed the demographic and clinical characteristics of all patients. Information about immediate postoperative and long-term trigeminal pain status was obtained from hospital charts and from letters that patients had been asked to write annually, after discharge from the hospital. When no long-term follow-up information was on file, patients were interviewed by telephone. Information about persistence or recurrence of pain, medication use, timing of relapse, and additional procedures performed was collected.

STATISTICAL ANALYSIS

Two groups of patients were defined for the purpose of data analysis. Group A included all patients (n=420) whose immediate postoperative trigeminal pain status was known. This group was used for the analysis of immediate postoperative outcome. The subset of group A (n=292) with immediate postoperative resolution of trigeminal pain and follow-up for 12 months or longer was defined as group B, which was used for the long-term outcome analysis and the development of a predictive model for pain recurrence. To validate the proposed model, we randomly divided group B into 2 subgroups in a two-thirds–one-third ratio. The larger subgroup was used for an analysis that determined the statistically significant factors for pain recurrence within each subgroup, whereas the smaller subgroup was used to validate the results of this analysis. The validation process consisted of 3 independent trials of group B division and analysis.

Predictive factors for immediate postoperative outcome were assessed by logistic regression analysis. The predictive model for long-term outcome was generated using Cox regression analysis and proportional hazard calculation. Factors considered as predictors in all analyses were the patient’s sex, age, side and trigeminal distribution of pain, duration of symptoms, prior percutaneous procedures, and presence of vascular compression as determined intraoperatively. Age and duration of symptoms were assessed as dichotomous variables, divided at a significant cutoff point to simplify the analysis. The logistic and Cox regressions included univariate analyses, followed by multivariate analysis, first looking at each pair of factors and their interaction and then including all factors and any significant interactions. A Kaplan-Meier survival plot was created for all patients with a postoperative follow-up of 12 months or longer. Time to recurrence of pain after a successful postoperative outcome was designated as the midpoint between the patient’s latest follow-up evaluation without pain and the next evaluation when recurrence of pain was reported. Sensitivity analysis included time to recurrence of pain. Minimum time is defined as the latest follow-up evaluation without pain and maximum time, as the first follow-up evaluation with pain recurrence. The results were similar and are not presented. Statistical significance for all analyses was defined as P=.05 (2-tailed).

formed in 586 patients. Eight patients had posterior fossa tumors, 12 had multiple sclerosis, and 106 had previously undergone 1 or more posterior fossa explorations. There was insufficient follow-up information for 102 patients. Group A consisted of 420 patients. The age and sex of the patients for whom no follow-up information was available were similar to those of the patients in group A. Group B consisted of 292 patients. Table 1 shows demographic and clinical characteristics for both groups. There were no differences in baseline characteristics between patients with and without long-term follow-up.

There were 225 MVD, 81 PSR, and 114 combination MVD and PSR procedures performed. After surgery, 98% (n=411) reported lessening of their pain, with 87% (n=367) experiencing complete pain relief and 13% (n=53) having some pain persistence.

Univariate and multivariate logistic regression analyses for immediate postoperative resolution of pain revealed pain on the left side (P=.007) and longer than 111/2 years’ duration of symptoms (P=.04) as significant predictive factors. Involvement of the V3 distribution of the trigeminal nerve was also a significant predictor (P=.04) in univariate analysis but was not significant in multivariate analysis (Table 2).

In group B, 76% (n=222) of the patients had complete pain relief and 90% (n=264) had lessening of pain at their latest follow-up evaluation. The mean duration of follow-up was 56.3 months for all patients followed up for longer than 12 months and 65.7 months for the subgroup that had no residual pain at their latest follow-up evaluation. The estimated likelihood of pain recurrence by 8 years was 34% (Figure 1).

Multivariate analysis revealed age younger than 53 years at the time of surgery (P<.001), duration of symptoms longer than 111/2 years (P=.04), and female sex and pain on the left side in men (P=.02) as predictors of long-term pain recurrence (Table 3). These factors remained significant in all 3 subgroup iterations (results not shown).
Based on the results of the multivariate analysis of long-term outcome predictors, we developed a model for predicting the risk of eventual recurrence of pain. Three risk groups were identified—high, moderate, and low risk—depending on the risk factors each patient possessed. Based on the hazard ratios, we defined female sex and pain on the left side in men as major risk factors, and symptom duration of 11½ years or longer and age younger than 53 years at the time of surgery as minor risk factors. The low-risk group included patients with only 1 minor risk factor (n=65). The moderate-risk group included patients with only 1 major risk factor (n=143). The high-risk group included patients with any combination of 2 or more risk factors (n=84) (Table 4). A survival curve according to risk group was then created, including all patients followed up for 12 months or longer (Figure 2).

For patients with immediate postoperative pain resolution, pain-free survival at 4 and 10 years, respectively, after surgery was 89%±4% at both end points for the low-risk group, 80%±4% and 71%±5% for the moderate-risk group, and 58%±6% and 47%±7% for the high-risk group (data are given as mean±SD). For all patients followed up for 12 months or longer, regardless of initial pain resolution, the mean pain-free survival at 4 and 10 years, respectively, was 87%±4% at both end points for the low-risk group, 77%±4% and 68%±5% for the moderate-risk group, and 56%±5% and 47%±6% for the high-risk group.

There were no perioperative deaths in this series. Major complications included hearing loss, hydrocephalus requiring a procedure to divert cerebrospinal fluid, anesthesia dolorosa, and intracranial hemorrhage (Table 5).

### Table 1. Demographic and Clinical Characteristics of 420 Patients Undergoing Surgical Exploration of the Posterior Fossa as Treatment for Idiopathic Trigeminal Neuralgia*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>420</td>
<td>292</td>
</tr>
<tr>
<td>Median age, y</td>
<td>63</td>
<td>63</td>
</tr>
<tr>
<td>Male sex</td>
<td>164 (39)</td>
<td>119 (41)</td>
</tr>
<tr>
<td>Left-sided pain</td>
<td>175 (42)</td>
<td>116 (40)</td>
</tr>
<tr>
<td>V1 only†</td>
<td>16 (4)</td>
<td>9 (3)</td>
</tr>
<tr>
<td>V2 only†</td>
<td>68 (16)</td>
<td>44 (15)</td>
</tr>
<tr>
<td>V3 only†</td>
<td>77 (19)</td>
<td>57 (20)</td>
</tr>
<tr>
<td>V1 and V2†</td>
<td>55 (18)</td>
<td>33 (11)</td>
</tr>
<tr>
<td>V2 and V3†</td>
<td>128 (31)</td>
<td>98 (34)</td>
</tr>
<tr>
<td>V1, V2, and V3†</td>
<td>59 (14)</td>
<td>40 (14)</td>
</tr>
<tr>
<td>Median duration of symptoms, mo</td>
<td>60</td>
<td>60</td>
</tr>
<tr>
<td>Previous procedure‡</td>
<td>70 (17)</td>
<td>50 (17)</td>
</tr>
<tr>
<td>Vascular compression§</td>
<td>340 (81)</td>
<td>240 (82)</td>
</tr>
</tbody>
</table>

*Data are given as number (percentage) of patients unless otherwise indicated.
†Refers to pain along the specified distribution only or in combination with other distributions.
‡Prior percutaneous procedure for the treatment of trigeminal neuralgia.
§The presence of vascular compression was determined intraoperatively.

### Table 2. Univariate and Multivariate Logistic Regression Analysis Results for Immediate Postoperative Resolution of Trigeminal Pain*

<table>
<thead>
<tr>
<th>P Value</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval for Hazard Ratio, Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Univariate</td>
<td>Multivariate</td>
</tr>
<tr>
<td>Age &lt;53 y</td>
<td>.10</td>
<td>.14</td>
</tr>
<tr>
<td>Female sex</td>
<td>.06</td>
<td>.13</td>
</tr>
<tr>
<td>Left-sided pain</td>
<td>.007</td>
<td>.005</td>
</tr>
<tr>
<td>Symptom duration &gt;11½ y</td>
<td>.04</td>
<td>.02</td>
</tr>
<tr>
<td>V1†</td>
<td>.26</td>
<td>.41</td>
</tr>
<tr>
<td>V2†</td>
<td>.64</td>
<td>.45</td>
</tr>
<tr>
<td>V3†</td>
<td>.04</td>
<td>.25</td>
</tr>
<tr>
<td>Previous procedure‡</td>
<td>.25</td>
<td>.83</td>
</tr>
<tr>
<td>Vascular compression§</td>
<td>.10</td>
<td>.37</td>
</tr>
</tbody>
</table>

*Variables are presented as the group that increased the likelihood for pain persistence. Multivariate analysis was performed including all variables simultaneously.
†Refers to pain along the specified distribution only or in combination with other distributions.
‡Prior percutaneous procedure for the treatment of trigeminal neuralgia.
§The presence of vascular compression was determined intraoperatively.
The recurrence of trigeminal pain after initial complete resolution is an issue that is often raised in the literature and in clinical practice. For patients who were pain free after surgery, the model of risk for the recurrence of pain described in this report predicts long-term pain status for low-, moderate-, and high-risk groups. Younger age,23 duration of symptoms,4,5,12 and female sex4,5,52 have been reported as predictors of long-term pain recurrence. The combination of male sex and pain on the left side has not been reported as predictors of long-term pain recurrence. The cause of this relationship is unclear.

Table 3. Univariate and Multivariate Cox Regression Analysis Results for Long-term Trigeminal Pain Recurrence

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>P Value</th>
<th>Hazard Ratio</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt;53 y</td>
<td>.002</td>
<td>2.2</td>
<td>1.6-4.7</td>
</tr>
<tr>
<td>Female sex</td>
<td>.08</td>
<td>1.6</td>
<td>1.3-11.2</td>
</tr>
<tr>
<td>Left-sided pain</td>
<td>.01</td>
<td>1.9</td>
<td>1.6-17.1</td>
</tr>
<tr>
<td>Sex/side</td>
<td>NA</td>
<td>1.4</td>
<td>0.1-0.78</td>
</tr>
<tr>
<td>Symptom duration &gt;11½ y</td>
<td>.27</td>
<td>1.4</td>
<td>1.0-3.7</td>
</tr>
<tr>
<td>V1†</td>
<td>.63</td>
<td>0.9</td>
<td>0.7-2.3</td>
</tr>
<tr>
<td>V2†</td>
<td>.82</td>
<td>1.1</td>
<td>0.2-13.2</td>
</tr>
<tr>
<td>V3†</td>
<td>.13</td>
<td>1.6</td>
<td>0.3-22.0</td>
</tr>
<tr>
<td>Previous procedure‡</td>
<td>.25</td>
<td>0.7</td>
<td>0.3-1.5</td>
</tr>
<tr>
<td>Vascular compression§</td>
<td>.19</td>
<td>0.7</td>
<td>0.4-1.5</td>
</tr>
</tbody>
</table>

*Sex/side signifies the interaction term between sex and side of pain. NA indicates not applicable. 
†Refers to pain along the specified distribution only or in combination with other distributions.
‡Prior percutaneous procedure for the treatment of trigeminal neuralgia.
§The presence of vascular compression was determined intraoperatively.

Table 4. Risk Factors and Their Hazard Ratios Included in the Model of Long-term Trigeminal Pain Recurrence

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Hazard Ratio</th>
<th>Risk Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt;53 y</td>
<td>2.8</td>
<td>Minor</td>
</tr>
<tr>
<td>Female/left</td>
<td>4.7</td>
<td>Major</td>
</tr>
<tr>
<td>Female/right*</td>
<td>3.9</td>
<td>Major</td>
</tr>
<tr>
<td>Male/left*</td>
<td>5.6</td>
<td>Major</td>
</tr>
<tr>
<td>Male/right*</td>
<td>1.0</td>
<td>None</td>
</tr>
<tr>
<td>Duration of symptoms &gt;11½ y</td>
<td>2.0</td>
<td>Minor</td>
</tr>
</tbody>
</table>

*Side of trigeminal pain.

Figure 2. Kaplan-Meier curve depicting pain recurrence, stratified according to risk group, for all patients with immediate postoperative resolution of pain and follow-up for 12 months or longer.

The recurrence of trigeminal pain after initial complete resolution is an issue that is often raised in the literature and in clinical practice. For patients who were pain free after surgery, the model of risk for the recurrence of pain described in this report predicts long-term pain status for low-, moderate-, and high-risk groups. Younger age,23 duration of symptoms,4,5,12 and female sex4,5,52 have been reported as predictors of long-term pain recurrence. The combination of male sex and pain on the left side has not been reported as predictors of long-term pain recurrence. The cause of this relationship is unclear.

We found no connection between long-term outcome and type of compression at the nerve root entry zone, a factor that previous studies4,6,17,52 have related to outcome. Our study is different from those, however, in that treatment was different for each patient, depending on the presence and type of compression. As others have previously observed,48 trigeminal neuralgia exists without significant compression of the nerve root, and in those cases we believe MVD to be inadequate treatment.

Posterior fossa exploration appears to be a safe treatment for trigeminal neuralgia. The most important morbidities of posterior fossa exploration include hearing loss (usually secondary to retraction injury to the cochlear nerve), development of hydrocephalus and cerebrospinal fluid leakage as a result of perioperative aseptic meningitis, cerebellar hemorrhagic stroke, and death. In a series of 4400 consecutive posterior fossa explorations for MVD of cranial nerves, McLaughlin et al21 reported complication rates as high as 0.9% for cerebellar injury, 2% for hearing loss, and 2.5% for clinically significant CSF leakage. The overall morbidity rates in our series are comparable to those previously published, and, unlike previous reports, this series involved no perioperative mortality. Although one may argue that a patient’s advanced age can lead to unacceptable morbidity, we withheld posterior fossa exploration only for absolute anesthetic contraindications. Therefore, our results reinforce the conclusion.
Trigeminal dysfunction, primarily dysesthesias, is the most common complication of the procedure, with an occurrence rate of 6% to 66%. There is an observed significant association between higher radiation dose and the development of trigeminal dysesthesias.

Stereotactic irradiation appears to be a promising treatment for typical trigeminal neuralgia, but it is not as effective in persistent complete pain relief as posterior fossa exploration. Given the significantly lower morbidity, it may be an appealing treatment in patients with recurrences following surgical exploration or with multiple medical problems and high anesthetic risks.

Our analysis has several limitations. Despite the prospective manner in which some of the follow-up data were obtained, it is a retrospective review. The treatment was not uniform, as 3 types of procedures were used. Although the number of patients represents the second largest published series of patients undergoing posterior fossa exploration for treatment of trigeminal neuralgia, the series is too small to permit a completely independent validation group for the prediction model or to identify risk factors that are less prevalent. The dichotomous presentation of the various predictors in the long-term outcome model does not adequately represent clinical practice. Uniform trends were identified in all the predictors along their range of values, but statistical considerations and the small size of the patient sample size made it necessary to include the most significant cutoff values in the model. We believe the model is illustrative of a continuous risk for pain recurrence, and it should be used with caution when applied to patients with characteristics close to the cutoff values.

Despite these limitations, we believe this analysis and the derived model are accurate. This is a large series of patients who underwent posterior fossa exploration for 29 years. The same surgeon performed all procedures, and the selection criteria for which surgery was performed remained unchanged throughout the series. With regard to the model, the primary analysis was supplemented with internal validation, which in all 3 iterations showed agreement in the model development and validation subgroups.

CONCLUSIONS

We report the outcome of posterior fossa exploration for trigeminal neuralgia and a validated model for risk stratification for eventual recurrence of trigeminal pain. We expect the model to be a useful instrument in more accurate decision making about treatment and in better counseling of patients with trigeminal neuralgia.

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