



Comparison of Prognostic Scoring Systems to Predict Durable Pain Relief After Microvascular Decompression for Trigeminal Neuralgia

Abdullah H. Ishaque¹, Haihan Xie², Hayden Danyluk^{3,4}, Blaise M. Wheatley³, Robert Broad³, Linglong Kong², Tejas Sankar³

■ **BACKGROUND:** Microvascular decompression (MVD) is an effective treatment for trigeminal neuralgia, but pain recurs in a substantial minority of patients. Two recently published scoring systems by Hardaway et al. and Panczykowski et al. use simple preoperative clinical and imaging features to predict durable pain relief following MVD, but their predictive performance has not been independently validated. This study aimed to compare predictive performance of the Hardaway et al. score (HS) and Panczykowski et al. score (PS) for 1-year, 3-year, and long-term pain-free outcomes after MVD for trigeminal neuralgia.

■ **METHODS:** HS and PS were computed for a retrospective, single-institution cohort of 68 patients with trigeminal neuralgia who underwent MVD. Primary outcome was pain recurrence after MVD. Predictive performance of HSs and PSs was evaluated with area under the curve sensitivity analysis and regression models for survival analyses at 1 year, 3 years, and last follow-up.

■ **RESULTS:** Area under the curve for predicting pain-free outcome was higher for PS versus HS at 1 year (0.873 vs. 0.775) and 3 years (0.793 vs. 0.704). Cox proportional hazard models showed that PS better predicted long-term pain-free outcomes compared with HS ($P < 0.05$). One-year pain-free outcome was best predicted by pain type; longer-term

outcomes were better predicted by presence and degree of neurovascular compression on preoperative imaging.

■ **CONCLUSIONS:** PS is superior to HS in predicting pain-free outcomes after MVD, which may aid in patient selection and counseling. Overall, more significant neurovascular compression of the trigeminal nerve root, and to a lesser extent classical paroxysmal pain, are good predictors of durable pain relief after MVD.

INTRODUCTION

Microvascular decompression (MVD) is a well-established treatment option for patients with trigeminal neuralgia (TN). While observational studies suggest that MVD is highly effective in providing long-term pain relief for TN,^{1,2} up to 25% of patients can experience recurrence of pain within 2 years after MVD with approximately 4% annual risk of recurrence.^{3,4} Identifying patients who are less likely to have durable pain relief after MVD is important to inform patient counseling and surgical decision making.

Numerous studies have been conducted to identify predictors of durable pain-free outcomes following MVD.^{2,5,6} Recently, 2 simple preoperative scoring systems, by Hardaway et al.⁷ and Panczykowski et al.,⁸ were independently developed to predict

Key words

- Microvascular decompression
- Outcome
- Prognosis
- Response
- Score
- Trigeminal neuralgia

Abbreviations and Acronyms

- BNI:** Barrow Neurological Institute
- CI:** Confidence interval
- HR:** Hazard ratio
- HS:** Hardaway et al. score
- MVD:** Microvascular decompression
- NVC:** Neurovascular compression
- OR:** Odds ratio

PS: Panczykowski et al. score

TN: Trigeminal neuralgia

From the ¹Faculty of Medicine and Dentistry, ²Department of Mathematical and Statistical Sciences, Faculty of Science, ³Division of Neurosurgery, Department of Surgery, Faculty of Medicine and Dentistry, and ⁴Division of Surgical Research, Department of Surgery, Faculty of Medicine and Dentistry, University of Alberta, Edmonton, Alberta, Canada

To whom correspondence should be addressed: Tejas Sankar, M.D.
[E-mail: tsankar@ualberta.ca]

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the durability of pain-free outcomes after MVD for TN using various individual clinical and radiographic risk factors. Both scores primarily take into account the type of pain experienced by patients before MVD (i.e., Burchiel type 1 or type 2⁹) and the presence and degree of neurovascular compression (NVC) at the trigeminal nerve on the affected side. The Hardaway et al. score (HS) incorporates type of TN, the presence of a vessel at the trigeminal nerve (vessel score), and a vessel compression severity score in its scoring scheme. The Panczykowski et al. score (PS) also includes the type of TN and the degree of NVC, but adds to this the preoperative response to antiseizure medication. While these scoring systems have shown potentially useful prognostic value, they have yet to be compared directly in an independent sample. The overall objective of this study was to compare the performance of these 2 preoperative scoring systems in predicting pain-free survival after MVD as a first-line surgical treatment of TN. To this end, we had 2 specific aims: 1) to analyze the ability of preoperative HS and PS to predict 1-year, 3-year, and long-term pain-free outcome and 2) to evaluate the predictive value for pain-free survival after MVD of individual risk factors within these scoring systems as well as others not included in these systems but that have been linked to response to MVD (specifically, symptom duration and sex^{1,10}).

MATERIALS AND METHODS

Study Participants

This retrospective study was approved by the local research ethics office. Our institutional operative database was searched to identify patients who underwent MVD for TN between 2007 and 2019 at a single center. Charts were reviewed in detail for all potential patients. Patients were included if they had a diagnosis of medically refractory Burchiel type 1 or type 2 TN⁹ and underwent first-time MVD. Patients were excluded if they had a history of previous neurosurgical procedures, a history of previous surgical procedures for treatment of TN (percutaneous trigeminal rhizotomy, stereotactic radiosurgery, or MVD), lesional TN, multiple sclerosis, unavailable high-resolution preoperative T2-weighted magnetic resonance imaging spanning the posterior fossa, or other concurrent NVC syndromes (e.g., hemifacial spasm). MVD was performed by 1 of 3 practicing neurosurgeons (authors B.M.W., R.B., and T.S.).

Data Collection

Demographic and clinical data including age at surgery, sex, TN signs and symptoms, and response to medication were retrospectively collected from patient charts. Patient consent was not obtained for the chart review, as this was not required. Preoperative high-resolution T2-weighted magnetic resonance imaging scans through the posterior fossa were evaluated for NVC by a neurosurgeon (T.S.) blinded to patient identity and outcome.

Preoperative Prognostic Scores

Preoperative prognostic HS and PS were calculated for all patients as outlined previously (Table 1).^{7,8} The HS ranges from 0 to 3, where all patients with type 2 TN receive a total score of 0 regardless of vessel and compression subscores.⁷ For patients with type 1 TN, NVC severity score is assigned based on the

Table 1. Preoperative Predictive Scores for Pain-Free Outcomes After Microvascular Decompression for First-Time Treatment of Trigeminal Neuralgia

	Points
Hardaway et al. score	
TN type	
1	1
2	0
Vessel score	
Artery or vein near trigeminal nerve	1
No vessel near trigeminal nerve	0
Compression severity score	
Compression or distortion of trigeminal nerve	1
Absence of vessel or vessel merely touching trigeminal nerve	0
Total	3
Panczykowski et al. score	
TN type	
1	1
2	0
Response to antiseizure medication	
Full and partial response	1
No response	0
NVC	
Arterial deformation	3
Arterial contact	2
No NVC or presence of a vein	1
Total	5

TN, trigeminal neuralgia; NVC, neurovascular contact.

degree of anatomical distortion of the trigeminal nerve graded on a 3-point scale: grade I indicates no deformity of the nerve root, grade II indicates compression of the nerve root by a vessel, and grade III indicates clear distortion of the nerve root by a vessel.^{11,12} The PS ranges from 0 to 5; in this scheme, NVC is classified in 3 categories: 1) absent NVC or presence of a vein, 2) arterial contact, or 3) arterial deformation. The individual components of the HS and PS were also used as individual risk factors to predict pain-free outcomes.

Outcome and Follow-Up

The primary outcome variable in this study was pain recurrence after MVD. Recurrent pain was defined as a Barrow Neurological Institute (BNI) pain intensity score of IIIB, IV, or V.¹³ Pain recurrence status was recorded at 1-year, 3-year, and last follow-up time points.

Outcome data were obtained from clinical charts; if outcomes were unclear, patients were contacted by telephone. Owing to the

coronavirus disease 2019 pandemic, explicit informed verbal consent was obtained for participation in follow-up data collection when patients were contacted over the telephone. Patients were asked a predefined series of questions from a script to avoid bias and to gather the same data as would be obtained from clinical charts. At least 3 separate telephone attempts were made to follow up with patients before classifying them as lost to follow-up. Date of pain recurrence was documented as the date of the clinic day when the patient first reported experiencing pain recurrence or the estimated date provided by the patient over the telephone follow-up. Patients were censored if they had not reached the outcome by the end of the study period (August 2020).

Statistical Analysis

Statistical analyses were conducted in MedCalc Statistical Software version 19.5.3 (MedCalc Software Ltd., Ostend, Belgium; <https://www.medcalc.org>) and in RStudio (RStudio: Integrated Development for R; RStudio, PBC, Boston, Massachusetts, USA; <http://www.rstudio.com/>). Normality was tested using the D'Agostino-Pearson test. The ability of the HS and PS to predict pain outcome was assessed using the average area under the receiver operating characteristic curve from 10-fold cross-validation. Decision curve analysis was performed to assess the utility of prognostic scores in supporting clinical decisions. Decision curve analysis is a method to assess the benefits of an intervention across a range of risks associated with undertreatment or overtreatment.¹⁴ Univariate and multiple logistic regression analyses were performed to investigate the relationship between individual risk factors and pain-free survival after MVD at 1- and 3-year time points. Survival analysis at last follow-up was conducted using univariate and multivariate Cox proportional hazards regression models. Kaplan-Meier survival analyses were used to compare differences in survival times. Statistical significance was accepted at $P < 0.05$ for all tests. For multivariate models, a stepwise method was used to enter independent variables if P was < 0.05 and variables were removed if P was > 0.1 .

RESULTS

Study Participant Characteristics

The study comprised 68 patients (30 men and 38 women with mean age 53.8 ± 11.0 years) who met the inclusion criteria. TN was right-sided in 43 cases; 1 patient had a prior history of bilateral type 1 TN, but underwent only right-sided MVD and was classified as having right-sided TN. All patients underwent a trial of medical treatment with carbamazepine or oxcarbazepine. Of 68 patients, 58 had type 1 TN and 10 had type 2 TN. **Table 2** presents demographic and clinical characteristics of the study sample.

Prognostic Scores

The distribution of HSs among patients is shown in **Figure 1**. There were 54 patients with vessel score 1 and 47 patients with compression severity score 1. The distribution of PSs among patients is also shown in **Figure 1**. There were 45 patients with a score of 1 for medication response. There were 24 patients with an NVC score of 1, 24 with a score of 2, and 20 with a score of 3. **Figure 2** shows the breakdown of individual HS and PS components.

Table 2. Study Sample Characteristics

Characteristics	Value
Number of patients	68
Age at surgery, years, mean \pm SD	53.8 \pm 11.0
Sex, number (%)	
Male	30 (44.1)
Female	38 (55.9)
Symptomatic side, number (%)	
Left	25 (36.8)
Right	43 (63.2)
Symptom duration, months, median (range)	48 (5–360)
Type of TN, number (%)	
1	58 (85.3)
2	10 (14.7)
TN, trigeminal neuralgia.	

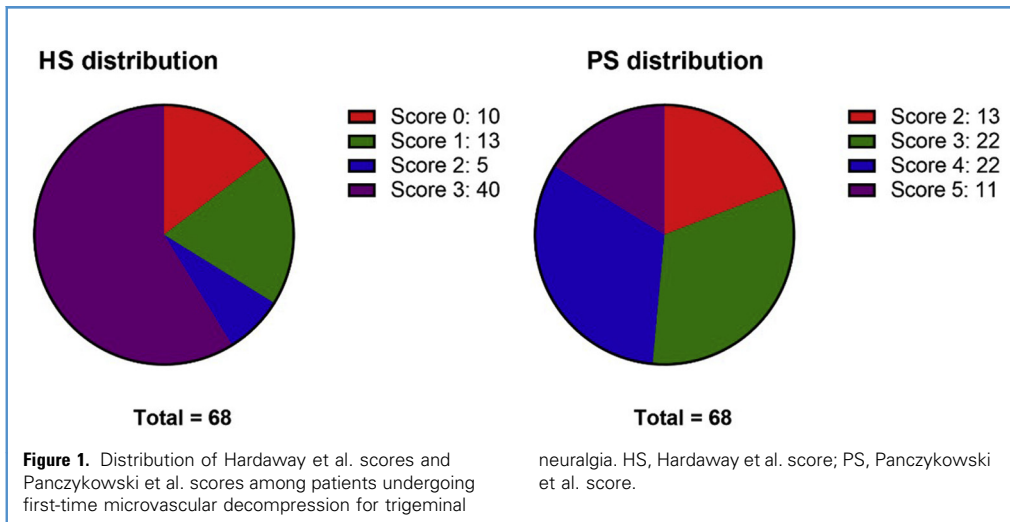
Outcome

Outcome data were available for 62 (91.2%) patients at 1-year follow-up. To obtain outcome data, 36 patients (52.9%) were reached via telephone; 6 patients could not be contacted. Outcome data were available for 53 (77.9%) patients at 3-year follow up. In 9 patients, it had not yet been 3 years since MVD, and these patients were excluded from the 3-year outcome analysis.

At 1 year, 14 patients experienced recurrence of pain, with median time to recurrence of 58 days (range, 14–303 days). Between 1 and 3 years, 13 patients experienced pain recurrence (median time to recurrence of 655.5 ± 180.8 days). Eight patients experienced pain recurrence after 3 years (**Figure 3**).

Survival Analysis: Pain Relief at 1- and 3-Year Time Points

Average area under the receiver operating characteristic curves for predicting pain-free outcome at the 1- and 3-year time points were higher for PSs (0.873 and 0.793, respectively) compared with average area under the receiver operating characteristic curves for HSs (0.775 and 0.704, respectively) with 10-fold cross-validation (**Table 3**). Predicting pain relief at 3 years was less accurate than at 1 year for both scoring schemes. When compared directly, there was no statistically significant difference between HSs and PSs in predicting pain-free outcome at the 1-year ($P = 0.2$) or 3-year ($P = 0.1$) time points. Univariate analysis identified TN type and NVC as significant predictors of pain relief at 1 year after MVD (**Table 4**): patients with type 1 TN and higher NVC score had higher odds ratios (ORs) for pain relief at 1 year (6.11 and 2.51, respectively). Notably, male sex also predicted pain relief at this time point (OR = 7.09), whereas symptom duration did not. Three years after MVD, higher NVC (OR = 3.58), higher vessel score (OR = 4.51), and higher compression severity score (OR = 3.86) significantly predicted sustained pain relief in univariate analyses (**Table 4**). On multivariate analysis, male sex (adjusted OR = 10.1) and higher NVC scores (adjusted OR =



3.36) were significant predictors of sustained pain relief at 1 year after MVD. At 3 years, only NVC score (OR = 3.58) significantly predicted pain relief in multivariate analysis.

Survival Analysis: Long-Term Pain Relief

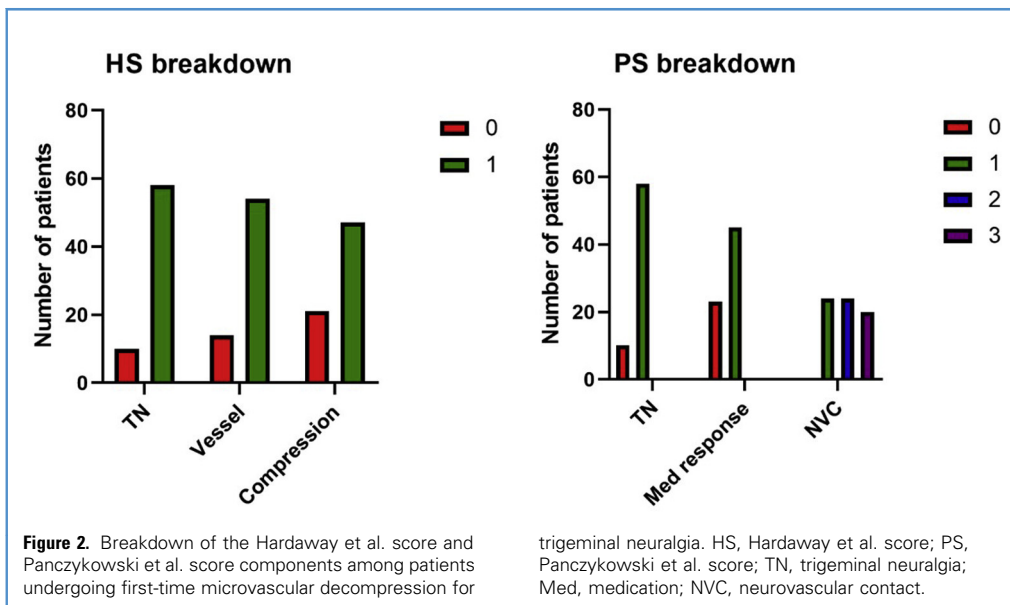
In the entire study period, 35 patients had pain recurrence, and 33 patients were censored. HSs (hazard ratio [HR] = 0.7, 95% confidence interval [CI] = 0.5–0.9) and PSs (HR = 0.5, 95% CI = 0.3–0.7) significantly predicted pain-free survival in univariate Cox proportional hazards regression models (P < 0.05). In multivariate analysis, however, only PSs significantly predicted pain-free survival (P < 0.05). Compression severity score (HR = 0.4, 95% CI = 0.2–0.8) and NVC (HR = 0.5, 95% CI = 0.3–0.8)

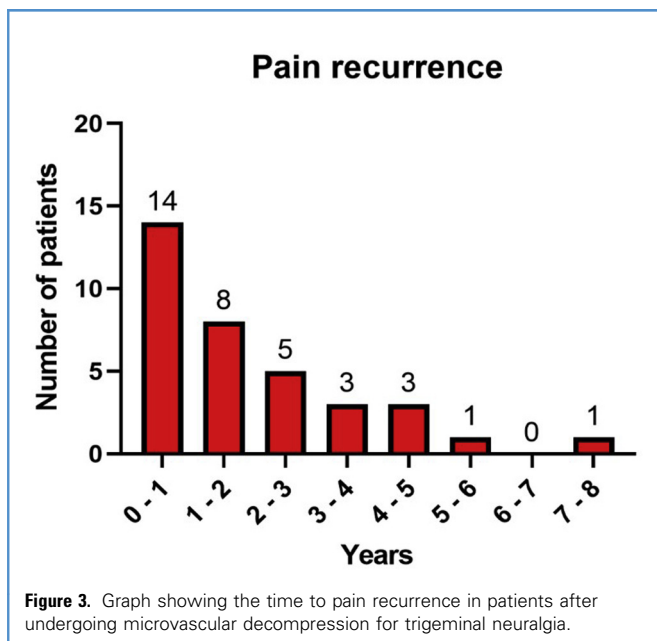
significantly predicted pain-free survival in univariate Cox proportional hazards regression models (P < 0.05). In multivariate analysis, only NVC significantly predicted pain-free survival (P < 0.05).

Kaplan-Meier survival analyses showed that preoperative HSs or PSs were significantly related to pain-free survival times after MVD (P < 0.05). Survival curves are shown in Figure 4, and average duration of pain-free survival by score is provided in Table 5.

Decision Curve Analysis

Decision curves evaluating the net reduction in the number of failed MVDs are shown in Figure 5. The decision threshold indicates a surgeon’s preference about performing MVDs after





weighing the potential benefit of treatment against the risk of unnecessary intervention. A lower decision threshold suggests that the surgeon sees benefit for the patient with MVD and is more likely to perform the surgery. In predicting 1 year of pain relief, the use of preoperative PS would reduce a greater number of unnecessary MVDs performed than HS for decision thresholds of up to 80%. For 3 years of pain relief, the PS again had a greater net reduction of MVDs than the HS, although to a lesser extent. The exact number of unnecessary MVDs prevented at each decision threshold is provided in [Table 6](#).

DISCUSSION

At 1- and 3-year time points, we found that the PS had higher accuracy compared with the HS at predicting pain-free outcome after first-time MVD for TN. In longer-term follow-up, PSs also better predicted length of overall pain-free survival. Furthermore, we found the PS had greater theoretical utility in preventing failed

MVDs. With respect to the individual risk factors, male sex (not included in either PS or HS) and higher NVC score predicted sustained pain relief at 1 year after MVD, with TN type also contributing significantly to pain relief at the 1-year time point in univariate analysis. Pain relief 3 years after MVD was best predicted by NVC score. We did not find that duration of TN before MVD was a significant predictor in our analyses.

The PS and HS are characterized by key differences. Unique to the HS, all patients with type 2 TN receive a score of 0 regardless of the nature and degree of NVC. This scheme biases against patients with type 2 TN and underweights patients who may actually respond to MVD. Previous studies have suggested that approximately one third of these patients may benefit from long-term pain-free outcomes following MVD.^{5,6} Additionally, the PS treats NVC in a more granular ordinal fashion, whereas the HS treats it as a binary variable. Indeed, for our patients, NVC subscores within the broader PS were evenly distributed, and this likely contributed to its improved accuracy in predicting short-term outcomes. Our data suggest that the degree of NVC as defined in the PS is a particularly sensitive marker for durability of pain relief after MVD.

There is a well-documented relationship between NVC and symptoms of TN.^{12,15-18} In particular, previous studies have shown that the degree of NVC is a significant predictor of pain relief after MVD.^{12,15,16} Another study showed that proximal atrophy of the trigeminal nerve, which was closely associated with the severity of arterial compression, correlated with improved pain relief following MVD.¹⁹ Unsurprisingly, we found that characteristics of neurovascular conflict (i.e., NVC and vessel score) appear to influence the durability of pain relief in the short and long term following MVD. Of note, we did not specifically evaluate the location of neurovascular conflict in relation to the root entry zone of the affected trigeminal nerve, as this was not a variable in either the PS or the HS scale, though previous publications¹⁵ have suggested that contacting or compressive vessels distal to the root entry zone are more likely to be associated with earlier pain recurrence after MVD.

The relationship between type of TN and pain relief following MVD is less clear-cut. Evidence suggests that patients with type 2 TN have worse outcomes than patients with type 1 TN.⁵ This could be related to an underlying difference in the pathophysiologic mechanism; a recent study showed differences in the microstructural integrity of the pontine segment of trigeminal

Table 3. Average Area Under the Curve Values for Hardaway et al. Score and Panczykowski et al. Score in Predicting Complete Pain Relief 1 and 3 Years After Microvascular Decompression for Trigeminal Neuralgia

	Time Point	Average AUC	SE	95% CI
HS	1 year	0.775	0.083	0.613–0.937
	3 years	0.704	0.089	0.529–0.879
PS	1 year	0.873	0.065	0.745–0.999
	3 years	0.793	0.080	0.635–0.950

Average AUCs were calculated using 10-fold cross-validation.

AUC, average area under the receiver operating characteristic curve; CI, confidence interval; HS, Hardaway et al. score; PS, Panczykowski et al. score.

Table 4. Univariate Logistic Regression Analysis for Durability of Pain Relief at 1 and 3 Years After First-Time Microvascular Decompression for Trigeminal Neuralgia in Relation to Various Preoperative Risk Factors

	Risk Factor	OR	95% CI	P Value
1 year	Type 1 TN	6.1	1.4–27.3	0.02*
	Vessel score	1.5	0.4–5.9	0.5
	Compression severity score	2.3	1.0–5.5	0.06
	Response to medication	1.8	0.5–6.2	0.3
	NVC	2.5	1.0–6.0	0.04*
	Male sex	7.1	1.4–35.2	0.02*
	Symptom duration	1.0	1.0–1.0	0.6
3 years	Type 1 TN	2.2	0.5–9.9	0.3
	Vessel score	4.5	1.1–18.9	0.04*
	Compression severity score	3.9	1.6–9.1	0.002*
	Response to medication	2.5	0.7–8.6	0.2
	NVC	3.6	1.6–8.1	0.002*
	Male sex	0.9	0.3–2.7	0.9
	Symptom duration	1.0	1.0–1.0	0.9

OR, odds ratio; CI, confidence interval; TN, trigeminal neuralgia; NVC, neurovascular contact.
*Significant result ($P < 0.05$).

root between type 1 and type 2 TN.²⁰ However, studies of larger sample sizes are needed to further delineate this association. In this study, we also found male sex to be predictive of short-term pain relief, but the exact basis of this finding remains unknown. Sex differences have been reported in descriptive studies that show a greater proportion of women without evidence of NVC²¹ and type 2 TN.²² More studies are needed to further explain this phenomenon.

A recent meta-analysis of 46 studies found that various features of neurovascular compromise, disease duration, and type of TN were factors associated with outcome following MVD for TN after an average follow-up of <2 years.¹⁰ Long-term predictors of pain relief after MVD remain understudied, and in this study we explicitly looked at pain outcomes ≥ 3 years after MVD. Some studies have shown that type 1 TN is a predictor of long-term pain relief,^{23,24} whereas others have found contradictory results.²⁵

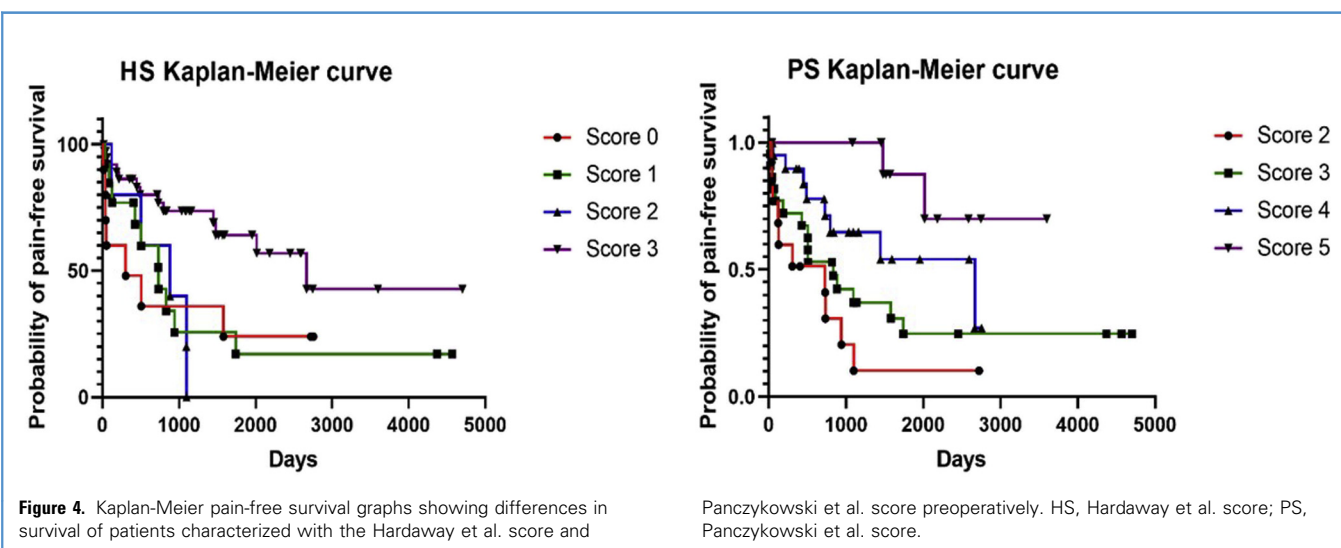


Table 5. Distribution of Patients Experiencing Pain Recurrence at 1- and 3-Year Time Points After Microvascular Decompression for Trigeminal Neuralgia Based on Hardaway et al. Score and Panczykowski et al. Score Schemes

	1-Year Time Point	3-Year Time Point
HS		
0	55.6	66.7
1	23.1	75.0
2	20.0	60.0
3	14.3	33.3
PS		
2	50.0	81.8
3	28.6	60.0
4	10.5	46.2
5	0	0

Data are presented as the percentage of patients experiencing pain recurrence with a given score for each scoring scheme at each time point.
HS, Hardaway et al. score; PS, Panczykowski et al. score.

These discrepancies are difficult to interpret because studies differ in their patient populations (e.g., including patients who underwent prior invasive procedures) and definition of successful postoperative pain relief (e.g., BNI score of II vs. III). Here, we defined pain relief as BNI score of IIIa or lower. The original BNI score of III was modified to IIIa and IIIb by Rogers et al.²⁶ to distinguish between patients who had no pain

postoperatively but were reluctant to discontinue medication (IIIa) versus patients who had recurrent pain that was controlled with medication (IIIb). In this categorization, some patients cannot be classified as better than IIIa despite experiencing no pain because of their hesitation to stop medication for fear of recurrent pain. Therefore, we did not consider the use of medication in the postoperative period as an absolute sign of treatment failure.

Prognostic scores can offer a simple, yet powerful tool to assist with clinical decision making in the management of patients with TN. Here, we showed that the PS can potentially reduce the number of unnecessary MVD surgeries and thus improve patient selection. Before this study, the 2 proposed predictive scoring systems thus far for TN had not yet been tested in independent cohorts. More studies are required to further validate the findings of our study.

This study is limited by its small sample size. There were only 10 patients with type 2 TN; therefore, we cannot generalize our findings to a larger population of patients with type 2 TN. Furthermore, the study was conducted using retrospective clinical data and telephone follow-up. This can potentially add uncertainty in the exact timeline of pain recurrence for certain patients. Future studies should focus on acquiring prospective data over a longer duration. Despite these limitations, our data show that the PS is better than the HS in predicting pain-free outcome after first-time MVD and may have clinical utility in helping surgeons counsel patients about the likelihood of success after MVD and help them come to a joint decision about whether to proceed with MVD.

CONCLUSIONS

Our findings confirm that the PS performs well in predicting pain-free outcomes up to 3 years after initial MVD in patients with TN.

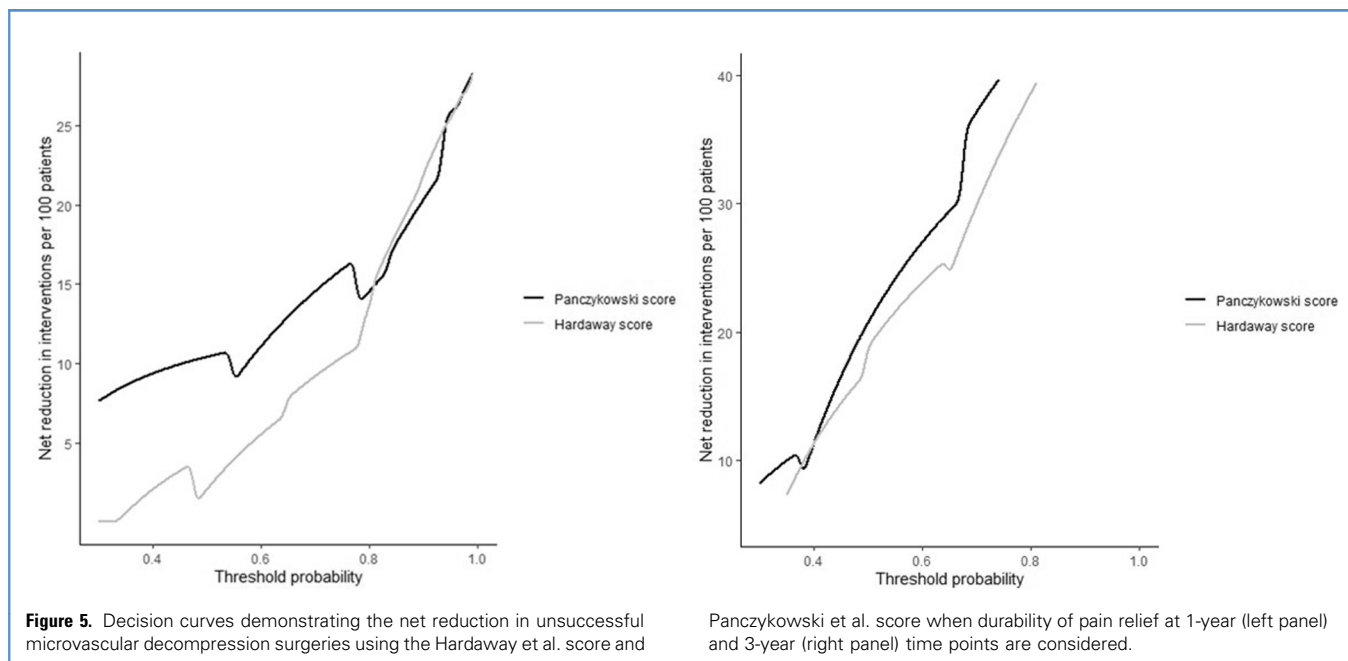


Table 6. Net Reduction in Microvascular Decompression Surgeries per 100 Patients for Pain-Free Outcomes as Predicted by Preoperative Hardaway et al. Score and Panczykowski et al. Score

Decision Threshold	1-Year Net Reduction in MVD		3-Year Net Reduction in MVD	
	HS	PS	HS	PS
0.40	2	9	11	11
0.50	2	10	18	20
0.60	5	11	23	27
0.70	9	14	29	37
0.80	13	14	38	42
0.90	21	20	45	45
0.99	28	28	50	50

MVD, microvascular decompression; HS, Hardaway et al. score; PS, Panczykowski et al. score.

The predictive ability of this scoring system is largely driven by a strong relationship between the degree of NVC of the trigeminal nerve root and durable pain relief after MVD.

CRedit AUTHORSHIP CONTRIBUTION STATEMENT

Abdullah H. Ishaque: Conceptualization, Methodology, Formal analysis, Investigation, Data curation, Writing – original draft.

Haihan Xie: Methodology, Formal analysis, Writing – review & editing, Visualization. **Hayden Danyluk:** Data curation, Writing – review & editing. **Blaise M. Wheatley:** Data curation, Writing – review & editing. **Robert Broad:** Data curation, Writing – review & editing. **Linglong Kong:** Methodology, Formal analysis, Writing – review & editing, Supervision. **Tejas Sankar:** Conceptualization, Methodology, Resources, Writing – review & editing, Supervision, Project administration, Funding acquisition.

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