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ALEXA-Y: A Proposed Pilot Score Framework for Predicting High-Impact Endoscopic Yield in Microvascular Decompression for Trigeminal Neuralgia and Hemifacial Spasm

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Abstract: Despite being a benign condition, neurovascular compression syndromes significantly impact the quality of life and social interactions in the majority of patients. The most frequently reported neurovascular compression syndromes are trigeminal neuralgia and hemifacial spasm, and the offending vessel is most commonly represented by an artery. The best therapeutic results were reported in patients undergoing microvascular decompression (MVD) surgery. Although the endoscopic-assisted MVD has been associated with better intraoperative visualization, improved detection of additional intraoperative conflicts, and fewer reported recurrences, currently, there is no existing tool that can assess in which cases the endoscope utilization can be of high impact. A single institutional retrospective pilot derivation study was conducted, based on statistical analyses of data collected from our consecutive patients, treated by MVD for trigeminal neuralgia and hemifacial spasm, between January 2020 and November 2025. A proposed predictive score framework named ALEXA-Y was developed, a priori, based on clinically accessible candidate domains and subsequently explored in a pilot derivation cohort. A total of 37 patients with trigeminal neuralgia and hemifacial spasm were included, out of which 19 patients treated with endoscope-assisted MVD were selected as the derivation cohort for the ALEXA-Y score. In 15.8% of the cases, a high-impact endoscopic yield was recorded. This study should be interpreted as hypothesis-generating due to the small number of outcome events. The present pilot study supports the ALEXA-Y concept as a clinically plausible multicomponent score framework for anticipating high-impact endoscopic yield. In our study, in the current derivation cohort, the L component demonstrated the strongest and the most stable predictive signal, while the remaining candidate domains should be further tested in larger cohorts.

Keywords: trigeminal neuralgia; hemifacial spasm; microvascular decompression; endoscopic-assisted surgery; predictive score

1. Introduction

Trigeminal neuralgia (TN) and hemifacial spasm (HFS) represent the most commonly reported neurovascular compression syndromes (NVCS), which can significantly impact the quality of life in many individuals [1]. Although in approximately 3% of the cases no neurovascular conflict can be identified, in more than 90% of patients the offender is an artery or a vein [2, 3]. The first-line therapeutic management in most of the NVCS comprises oral medication, and in cases of recurrence or refractory symptoms, minimally invasive procedures can be effective in the short term [4, 5]. Microvascular repositioning techniques were also reported, using fibrin glue or Prolene slings, with very good outcomes [6-8]. Nevertheless, when it comes to long-term best results, MVD has been proven superior, especially when endoscopically assisted [9].

In the last decades, the endoscopy gained more attention in NVCS, whether it is just MVD-assisting or full-endoscopic MVD. Its significance has been proven, especially in better visualization, "around-the-corner", and identifying hidden neurovascular conflicts [10, 11], although some studies report similar results in patients treated with classical versus endoscopic MVD [12]. However, to date, there is no existing method to assess in which cases the endoscope utilization can really be of high impact, and the current article aims to identify the main factors that will predict the endoscopic yield in MVD for TN and HFS. By identifying these factors, we aim to create an exploratory risk score that can be further validated in larger cohorts.

2. Materials and Methods

The current article is a single-institutional retrospective pilot derivation study that includes 37 consecutive patients treated for TN and HFS in the Neurosurgical Department of Clinical Emergency Hospital "Bagdasar-Arseni", Bucharest, Romania, between January 2020 and November 2025. The derivation cohort used for creating a predictive score included 19 patients (only cases treated with endoscopic-assisted MVD, where the endoscopic yield can be measured). For endoscopic assistance, we used the QEVO® micro-inspection tool, attached to the Zeiss Kinevo 900 operating microscope, which is available at our institution. The study was approved by the Research Ethics Committee of “Bagdasar-Arseni” Clinical Emergency Hospital (No. 2674/22.01.2026). We collected data from the hospital’s databases and individual medical records. To select the patients, we interrogated the hospital’s digital databases for the terms „neurovascular compression syndrome”, „trigeminal neuralgia”, and „hemifacial spasm”. Subsequently, we evaluated each patient's physical records and conducted a detailed evaluation of their data.

The inclusion criteria were: 1) adult patients over 18 years old, with a confirmed diagnosis of TN or HFS; 2) patients who underwent MVD surgery at our institution, performed by neurosurgeons with similar training and surgical expertise, regardless of whether the patients had previously undergone other treatment procedures; 3) availability of intraoperative data, including endoscopic assistance in a subset of patients. The exclusion criteria included: 1) insufficient clinical, imaging, or operative data; 2) diagnosis of both TN and HFS in the same patient; 3) secondary causes of TN or HFS.

We defined high-impact yield as cases in which endoscopy effectively changed the intraoperative strategy and/or identified hidden offenders that were previously unseen or unclear when assessed by microscopy only. In these cases, a score of 1 point was applied; otherwise the score was 0 (endoscopy was only confirmatory).

Given that a shorter duration of symptoms was associated with high-impact yield, we defined a binary point assignment with 1 point for a duration of less than or equal to 24 months. This specific duration is a data-driven threshold and is clinically interpretable.

3. Results

3.1. Statistics and Replicability

After selecting the patients who fulfilled the inclusion criteria, data containing clinical and paraclinical features, clinical course, therapeutic strategies, and outcomes were assessed. The collected data were coded/parsed and analyzed using Microsoft Excel version 16.89.1, Python 3.10.11 (Thonny 4.1.7), and GraphPad Prism version 10.2.1. Statistical significance was defined as a p-value<0.05, while analyses involving rare outcomes and small subgroup sizes were interpreted as exploratory and hypothetical. All collected data were anonymized to protect patient confidentiality and ensure compliance with ethical research standards.

After performing statistical correlations, we selected the most relevant variables in order to develop a predictive score for the high-impact endoscopic yield in MVD for TN and HFS. The candidate variables were selected based on clinical relevance and medical literature, but the final model was parsimonious given the small number of high-impact events.

3.2. Cohort characteristics and correlation analysis

A total of 37 patients were included in the initial statistical analysis in order to find significant statistical correlations. The demographic profile and cohort characteristics from our study are summarized in Table 1.

Table 1. Summary of demographic profile and cohort characteristics from our study.

Characteristic	Overall cohort (TN and HFS, N=37)
Demographics	
Age, years (mean +/- SD)	57.6 +/- 11.5
Age, years (median [IQR])	57.0 [49.0-67.0]
Female sex, n (%)	22 (59.5%)
Diagnosis	
Trigeminal neuralgia (TN)	32 (86.5%)
Hemifacial spasm (HFS)	5 (13.5%)
Clinical characteristics	
Left side affected by NVCS	20 (54.1%)
Symptom duration, months (median [IQR])	48.0 [12.0-84.0]
Symptom duration, months (range)	2.0-180.0
Smoking status	
Smoking reported	29 (78.4%)
Ever-smoker (current/former)	12 (41.4%)
Never smoker	17 (45.9%)
Current smoker	10 (27.0%)
Former smoker	2 (5.4%)
Not reported	8 (21.6%)
Comorbidities	
Any comorbidity	28 (75.7%)
Hypertension	15 (40.5%)
Dyslipidemia	6 (16.2%)
Diabetes mellitus	3 (8.1%)
Cardiovascular disease	4 (10.8%)
History of stroke	1 (2.7%)
Thyroid disease	2 (5.4%)
Depression/anxiety	2 (5.4%)
Obesity	1 (2.7%)
Other comorbidity	1 (2.7%)
Previous interventions	
Any previous intervention	20 (54.1%)
Prior MVD	3 (8.1%)
Prior rhizotomy/destructive procedure	9 (24.3%)
Local infiltrations	3 (8.1%)
Prior Gamma Knife	2 (5.4%)
Prior botulinum toxin	5 (13.5%)
Other interventions	3 (8.1%)
Imaging and intraoperative conflict type	
MRI conflict type	
Arterial	35 (94.6%)
Venous	1 (2.7%)
No visible conflict	1 (2.7%)
Intraoperative conflict type	
Arterial	27 (73.0%)
Venous	9 (24.3%)
Arachnoid adhesions only	1 (2.7%)

Perioperative and follow-up characteristics were summarized in Table 2.

Table 2. Summary of perioperative and follow-up characteristics in our study population; * only in patients with TH; **in patients with TN and HFS; ***BNI (Barrow Neurological Institute) pain intensity score values were coded for statistical analysis, but were presented in the table using original categories (I-V; IIIa/IIIb where applicable); +PGIC (Patient Global Impression of Change) scale was recorded on the study's numeric scale from 1 to 4, with lower scores indicating greater improvement.

Characteristic	Overall cohort (TN and HFS, N=37)
Perioperative management	
QEVO micro-inspection used	19 (51.4%)
QEVO timing (among QEVO cases)	
Exploration and final inspection	14 (73.7%)
Final inspection only	5 (26.3%)
MVD material	
Teflon	34 (91.9%)
Alternative padding	1 (2.7%)
Other (arachnolysis/coagulation)	2 (5.4%)
Early postoperative outcome at discharge	
Complete relief	34 (91.9%)
Partial relief	1 (2.7%)
No relief	2 (5.4%)
Postoperative complications	
Any early postoperative complication	11 (29.7%)
Persistent complication (trigeminal hypoesthesia)	1 (2.7%)
Transient complications	10 (27.0%)
Selected complications	
CSF leak	4 (10.8%)
Meningitis	1 (2.7%)
Suture granuloma	2 (5.4%)
Facial palsy	1 (2.7%)
Diplopia	1 (2.7%)
Abducens palsy	1 (2.7%)
Cerebellar ischemia	1 (2.7%)
Trigeminal hypoesthesia	1 (2.7%)
Follow-up and long-term outcomes	
Follow-up duration, months (median [IQR]) (N=34)	28.5 [11.6-42.3]
Follow-up duration, months (range) (N=34)	1.0-56.4
Recurrence during follow-up	4 (10.8%)
Reintervention (repeat MVD)	2 (5.4%)
Reintervention (Gamma Knife)	1 (2.7%)
Patient-reported and pain outcomes	
BNI* at last follow-up (median [IQR]) (N=29)	I [I-I]***
BNI at last follow-up (range) (N=29)	I-IIIa***
PGIC** at last follow-up (median [IQR]) (N=34)	1 [1-1]
PGIC at last follow-up (range) (n=34)	1-4+

3.2.1. Age analysis

The mean age in our study group was 57.6+/- 11.5 years, while the median [IQR] age was 57.0 [49.0-67.0] years. In the TN group, the mean age was 59.2 +/- 11.0 years, and in the HFS group, the mean age was 47.4 +/- 9.7 years (p=0.0431). In the derivation cohort (TN and HFS), in 3 cases, there was a high-impact yield (median age 54.0 years), and in 16 cases, there was no high-impact (median age 54.5 years); p=0.654. When comparing the age between the cases with high-impact endoscopic yield and those with no impact (only confirmation) in the QEVO derivation cohort, we found that there was no statistically significant association between the ages in those 2 groups (Figure 1).

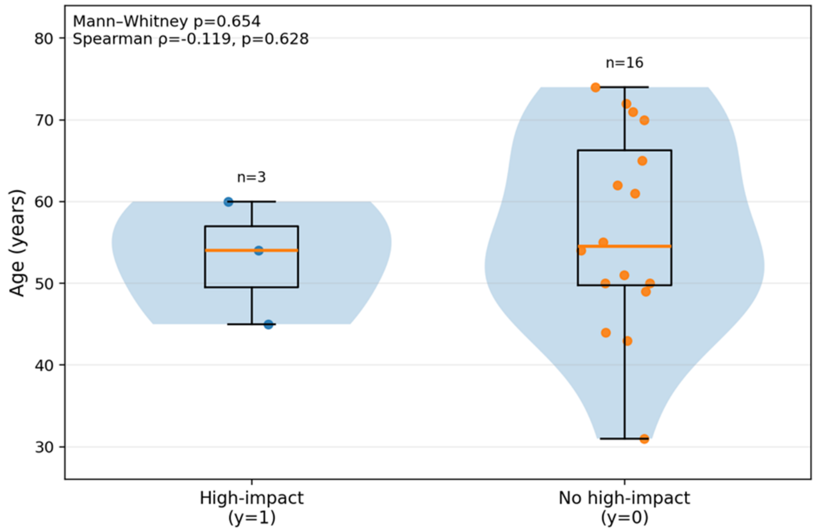

Figure 1. Age distribution by high-impact endoscopic yield status in the QEVO derivation cohort. The individual values are shown with violin and boxplots; no significant difference was observed in age between high-impact and no-impact cases (p=0.654), and age was not correlated with yield status (p=0.628).

When performing the receiver operating characteristic (ROC) curve analysis in order to evaluate age as a predictor of high-impact endoscopic yield in the QEVO derivation cohort, we found that the discriminative performance was poor (area under the curve - AUC=0.594), with wide uncertainty (bootstrap 95% CI 0.300-0.882), which indicates that age is not a reliable predictor of high-impact yield in this pilot cohort (Figure 2).

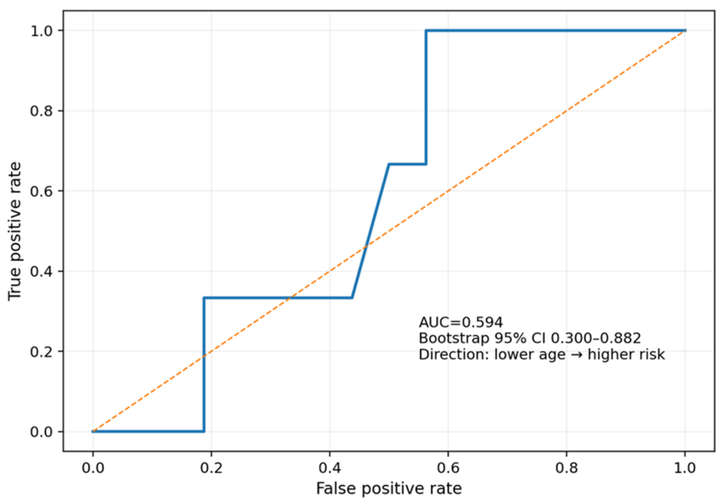

Figure 2. ROC curve assessing age as a predictor of high-impact endoscopic yield in the QEVO cohort (N=19).

3.2.2. Length of symptoms

When we analyzed the duration of the symptoms in the QEVO derivation cohort (N=19) in order to evaluate how many cases were impacted by the endoscope utilization, we found that 3 cases had a high-impact yield (score y=1) and 16 cases had no impact (score y=0). High-impact groups had a shorter symptom duration, with borderline p-values (Figure 3).

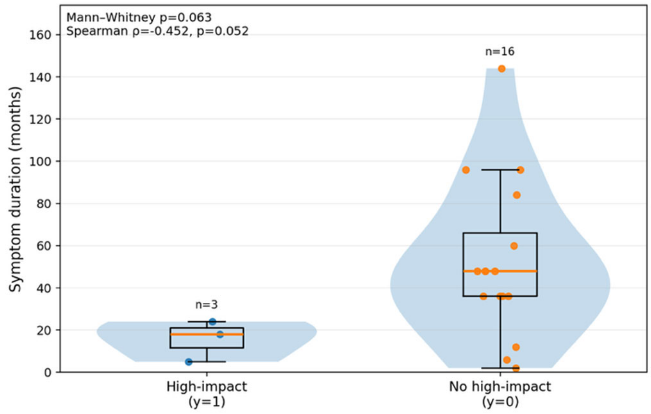

Figure 3. Symptoms duration associated with high-impact yield in our derivation cohort (N=19).

The ROC curve evaluating the duration of symptoms as a predictor of high-impact endoscopic yield in the QEVO derivation cohort demonstrated a good discrimination (AUC=0.854; bootstrap 95% CI 0.667-1.000) (Figure 4).

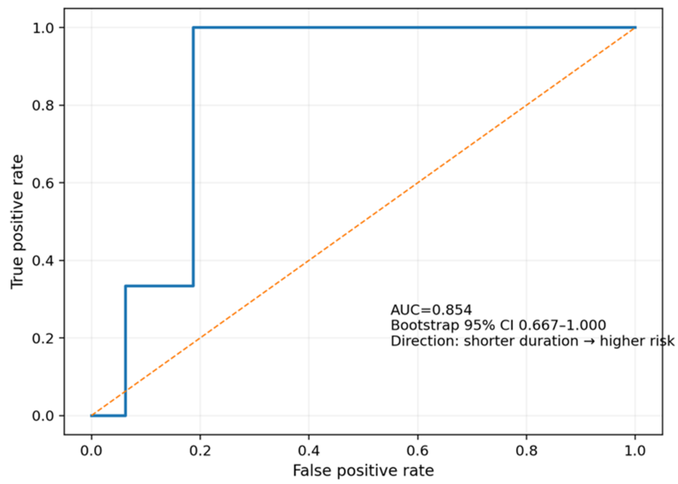

Figure 4. Symptom duration as a predictor of high-impact yield (ROC).

Given the pilot sample size, we evaluated both association (group comparison) and discriminative performance (ROC/AUC), and derived a simple cut-off-based score for risk stratification. The defined data-driven cut-off was equal to or less than 24 months (Figure 3). A score of 1 point was given if the length of symptoms was less than or equal to 24 months, and a score of 0 points was given if the symptoms were more than 24 months. Using the established cut-off, the score stratified high-impact yield from 0/13 in score 0 to 3/6 in score 1 (Fisher exact p=0.021).

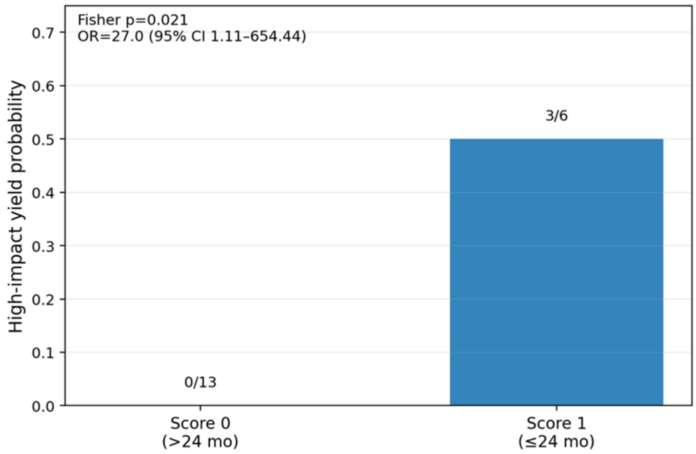

Figure 5. Risk stratification of high-impact endoscopic yield in the QEVO derivation cohort; cut-off equal to or less than 24 months; p=0.021.

3.2.3. Endoscopy

In our cohort derivation (N=19), we have 14/19 patients (73.7%) in whom the endoscopy was used for exploration and final inspection (timing=3), and 5/19 (26.3%) patients in whom the endoscopy was used for final inspection only (timing=2). The high-impact cases were present in the timing 3 group (3/14, 21%), but the correlation was not statistically significant, p=0.530, most likely due to the small sample size (Figure 6). Timing=1 was applied only if the endoscope was used for exploration solely at the beginning of the intervention.

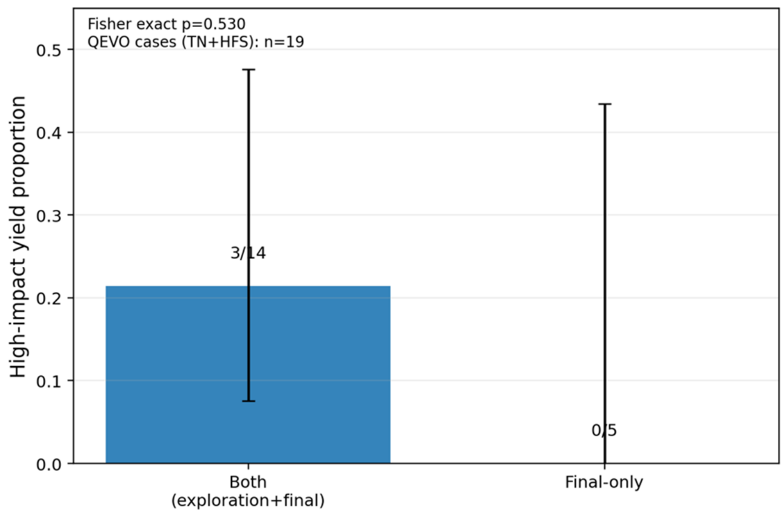

Figure 6. High-impact endoscopic yield by QEVO timing in the derivation cohort.

When comparing the duration of symptoms (months) with QEVO timing, we concluded a median in the timing 3 group of 36.0 months, and a median of 84.0 months in the timing 2 group, p=0.0316 (Figure 7). In our cohort, QEVO was used both at the beginning and at the end of the neurosurgical intervention, especially in patients with more recent symptoms, while in patients with a longer duration of symptoms, the endoscope was used more frequently at the end of the surgery. This suggests that the timing is not random, and it is impacted by the case profile.

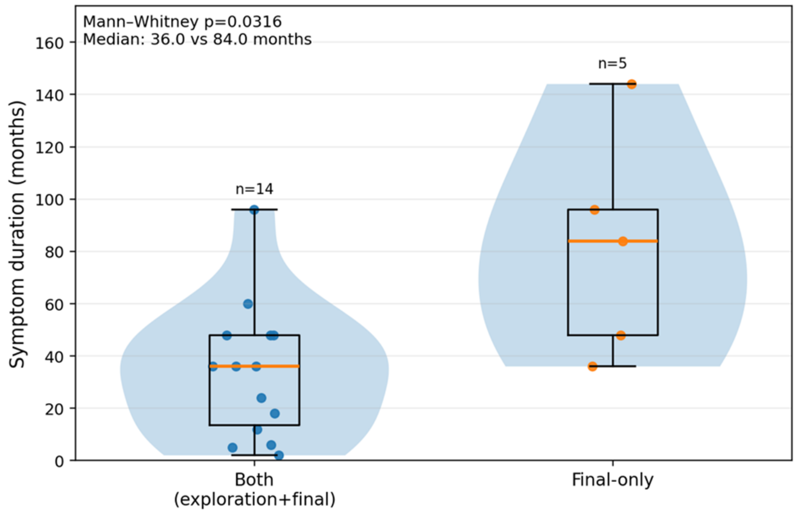

Figure 7. Comparison of the duration (months) of QEVO endoscope use (exploration and final versus final-only) in the derivation cohort.

3.2.4. Smoking status

In our study population, out of 37 patients, 29 (78.4%) had a reported smoking status. A total of 41.4% of the patients are current or former smokers (27%, 5.4%), while 45.9% of the patients never smoked. When correlating smoking status with different variables, we identified several associations. Only the statistically significant results were selected and are shown in Table 3.

Table 3. Statistically significant analyses regarding smoking status in our study population; *CI is very large because the number of patients with HFS is very small (that is why the correction is 0.5).

Smoking exposure	Outcome/Variable	Cohort (N)	Result (effect)	p-value
Ever-smoker (current/former) vs never	Age (years)	29	Median 48.5 (ever) vs 60.0 (never)	0.0167
Ever-smoker (current/former) vs never	Diagnosis (HFS vs TN)	29	OR 18.53 (95% CI 0.89-385.25)*	0.0208
Smoking category (Never/Former/ Current)	Diagnosis (HFS vs TN)	29	Distribution (counts): TN=17/0/8; HFS=0/2/2	0.0019
Smoking category (Never/Former/ Current)	Age (years)	29	Medians: Never 60.0; Former 48.5; Current 49.5	0.0479
Ever-smoker vs never (adjusted)	Diagnosis (HFS vs TN) adjusted for age and sex	29	Adjusted OR 3.25; bootstrap 95% CI 1.58-6.05	(CI excludes 1)

In our study population, 19 patients were treated by endoscopy-assisted MVD, out of which 14 had a reported smoking status. In the QEVO derivation cohort with reported smoking status, the high-impact event results were 2/7 in the never-smoking group and 1/7 in the former/current smoking group (Figure 8); p=1.000.

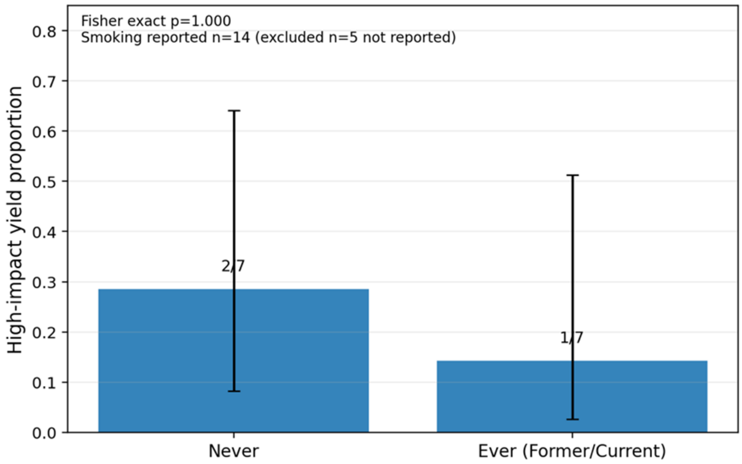

Figure 8. High-impact yield by smoking status in our study population.

A total of 17 patients never smoked, 2 were former smokers, and 10 patients were current smokers. When distributed by age, we found that there is a statistically significant difference between the 3 groups (Figure 9).

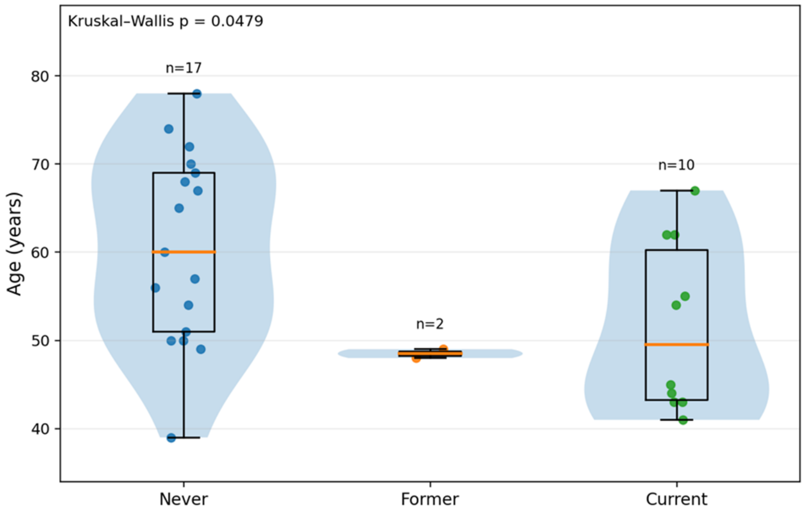

Figure 9. Age by smoking category - never, former, and current smoker; p=0.0479.

3.2.5. Associated comorbidities

In the derivation cohort, 4 patients had no reported comorbidities, while 15 had reported associated comorbidities. In the first group, in 1 patient, a high-impact yield was reported (1/4, 25%), while in the second group, in 2 patients, a high-impact yield was reported (2/15, 13.3%), but the analysis was not statistically significant, p=0.530 (Figure 10).

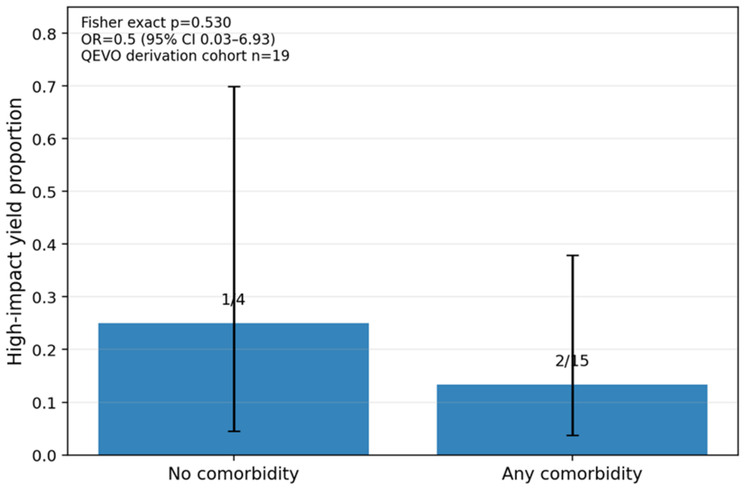

Figure 10. High-impact endoscopic yield by comorbidities in our cohort derivation; p=0.530.

After comparing the age of patients with comorbidities versus those without comorbidities, we found that patients with comorbidities are generally older; p=0.016. When the age increases, the probability of any comorbidity also increases, p=0.010 (Figure 11).

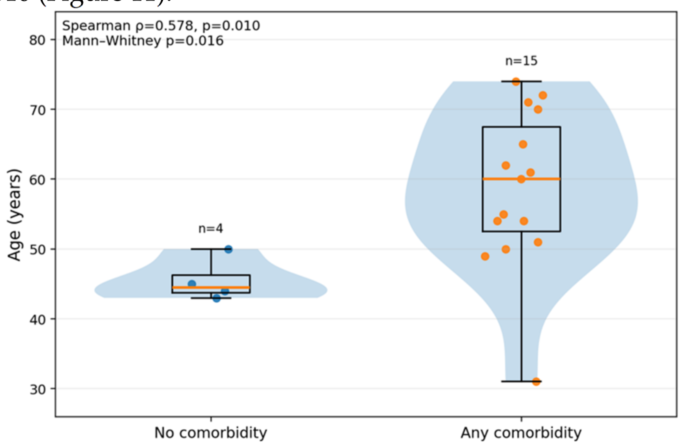

Figure 11. Age versus comorbidity in the QEVO derivation cohort.

4. Discussion

4.1. What Is the Endpoint (Y) Predicted by the Alexa Score?

Despite being very common in many MVD interventions in the last decade, the impact of endoscope utilization is yet to be assessed. Given that currently, there is no method that evaluates in which cases this adjuvant tool can be of high impact, the authors of this study aim to identify the main factors that will predict the endoscopic yield in MVD for TN and HFS. By identifying these factors, we aim to create a risk score that can be further validated in larger cohorts. It is very important to explain how we defined "high-impact yield" in our study. Therefore, these terms refer to a high-impact endoscopic yield, which are specifically the cases when QEVO endoscopy not only confirms a neurovascular conflict, but effectively changes something significant intraoperatively. A high-impact 1 score was applied when endoscopy led to a change in the intraoperative neurosurgical strategy (e.g., supplementary decompression, repositioning, identification of another conflict, etc.), and/or when endoscopy identified a hidden offender that was unseen or unclear when assessed by microscopy only. A high-impact 0 score was applied when endoscopy was only confirmatory of adequate MVD, without revealing hidden offenders or leading to any change in the intraoperative neurosurgical strategy.

According to Table 1, preoperative MRI classified the neurovascular conflict as arterial, venous, and no clearly visible conflict. However, intraoperative inspection revealed different mechanisms in some cases (a different offender or only arachnoid adhesions). We considered this discrepancy an MRI-intraoperative mismatch. We deliberately did not include the MRI-intraoperative mismatch as a candidate variable in the ALEXA-Y framework because it is not strictly a preoperative variable. Not only it becomes fully evident in the intraoperative settings, but also the concept overlaps with the definition of high-impact endoscopic yield which captures endoscopy-driven identification of additional findings beyond the initial preoperative expectation.

4.2. Assessing Potential Predicting Factors for the Score

Age (A)

An important candidate variable for predicting high-impact endoscopic yield in our derivation cohort is represented by patients' age. In order to assess whether this is a good variable to be included in the predictive score, we compared the distribution of age between high-impact cases and confirmation-only cases, while evaluating discriminative performance using ROC analysis (AUC with bootstrap confidence intervals). When comparing the age between the cases with high-impact endoscopic yield and those with no impact (only confirmation) in the QEVO derivation cohort, we found that there was no statistically significant association between the ages in those 2 groups. No monotonic association between age and high-impact yield probability was discovered. This concludes that, in our QEVO cohort (N=19), age does not seem to predict a high-impact endoscopic yield.

In the medical literature, age is often used as a predictive factor in various analyses. For instance, Tugened et al. demonstrated that in patients with TN, age over 45 years predicted long-term pain freedom without medication after MVD [13]. In like manner, Noorani et al. concluded that older age is a predictor of a good outcome in percutaneous surgery for TN [14]. Age was also a predictor of postoperative pain recurrence in the V1 branch nerve of the trigeminal nerve [15], and, along with procedure and duration of pain, could predict recurrence after surgery on the V3 branch [16].

In HFS, the age of symptom onset less than 45 years was associated with a more rapid progression [17], while younger age at surgery and older age at symptom onset led to a rapid progression and poorer postoperative outcomes [18]. In a recent article, Wang et al. stated that age was a significant predictor of short and long-term postoperative outcomes [19].

Length of symptoms (L)

Another promising candidate variable for predicting high-impact endoscopic yield in our derivation cohort is the length of symptoms in patients with TN and HFS. The symptom duration was defined as the time from the onset of symptoms until the neurosurgical intervention, and was recorded in months.

A high-impact yield appears especially in patients with a more recent symptomatology. After comparing the distribution of the symptoms duration between the 2 impact groups, we found that $p=0.063$. Although the value is not statistically significant, we can see a trend, as there is a tendency that symptoms duration are smaller in the high-impact group. After testing the monotonic association between symptom duration and high-impact, we obtained a negative ϱ (-0.452), which means that the higher the duration of symptoms, the lower the high-impact probability. Given that $p=0.052$, the results are not statistically significant but could be defined as borderline. The ROC curve evaluating the duration of symptoms as a predictor of high-impact endoscopic yield in the QEVO derivation cohort demonstrated a good discrimination

(AUC=0.854; bootstrap 95% CI 0.667-1.000). These results indicate that shorter symptom duration is associated with a higher probability of high-impact yield. In the majority of the comparisons, a patient with high-impact yield has a shorter symptom duration than a patient without high-impact. Symptoms with a duration of less than or equal to 24 months were associated with a higher probability of high-impact endoscopic yield - score 1 (3/6, 50%) in comparison to more than 24 months - score 0 (0/13, 0%), and the results were statistically significant.

Symptom duration in the medical literature has also been demonstrated to be a predictive factor in many studies. A meta-analysis by Holste et al. concluded that a symptom duration of less than 5 years is a significant predictive factor of pain freedom after MVD in TN patients [20]. Similarly, it has been stated that longer symptom duration was associated with a higher recurrence rate after MVD [21] and poorer outcomes [22], while a shorter symptom duration in TN patients was a predictor for favorable long-term outcomes [23]. The results were similar when reported in patients with HFS [24-26].

Endoscopy (E)

In our database, the code was attributed as follows: timing 1 for exploratory use (of endoscopy) only if the endoscope was used solely at the beginning of the intervention; timing 2 for final inspection only if the endoscope was used solely at the end of the intervention, to verify the results; and timing 3 for exploration and final inspection, if the endoscope was used both at the beginning and at the final of the neurosurgical intervention. Our cohort concluded 14 cases with timing 3, 5 cases with timing 2, and no cases with timing 1. When we analyzed whether high-impact appears more frequently in both versus final-only endoscopic use, we found that in 3/14 high-impact cases were in the both group (timing 3), while 0/5 high-impact cases were registered in the final-only group. However, p=0.530, therefore the results were not statistically significant.

When analyzing timing versus the length of symptoms, we concluded a median symptom duration of 36 months in the timing 3 group and a median of 84 months in the timing 2 group, p=0.0316. These results show that in our cohort, cases where the endoscopy was used both at the beginning and at the end of the neurosurgical intervention had a more recent symptomatology.

A summary of the predictive value of endoscopy in MVD for NVCS in the medical literature is presented in Table 4.

Table 4. Summary of relevant articles in the medical literature regarding the importance and the predictive role of endoscopy in MVD for NVCS.

Study	Type of NVCS	Role of endoscopy	Predictive or prognostic component
Sandell T et al., 2014 [27]	TN	The endoscope was particularly useful when the neurovascular conflict was hidden by bony anatomy or located distally	Preoperative MRI predicted the need for endoscopy; the fraction of trigeminal nerve visible under microscopic view showed strong predictive value
Peng W et al., 2024 [28]	TN	Full-endoscopic MVD was assessed as a treatment for TN, with emphasis on postoperative recurrence	The authors developed a predictive nomogram for 1-year recurrence after full-endoscopic MVD
Yu G et al., 2024 [11]	TN	Compared endoscopic versus microscopic MVD; the endoscopic approach was safe and effective, with shorter decompression time	Shorter disease duration and severe neurovascular conflict were associated with better prognosis in the endoscopic group

El Refaee E et al., 2013 [29]	HFS	Intraoperative endoscopy was used as the reference standard for identification of the offending vessel in HFS	Preoperative 3D MRI had predictive value for conflict anatomy and offending-vessel identification.
Flanders TM et al., 2018 [30]	HFS	Demonstrated that fully endoscopic MVD is safe and effective for HFS and allows comprehensive visualization of the neurovascular conflict	Intraoperative resolution of the lateral spread response predicted greater clinical improvement
Ghaffari-Rafi A et al., 2023 [31]	HFS	Showed that endoscopic assistance increases the detection of multiple offending vessels	Longer symptom duration was associated with poorer outcome; endoscopy improved identification of multivessel conflicts
Peng W et al., 2023 [32]	TN and HFS	Showed that fully endoscopic MVD is safe and effective across several neurovascular compression syndromes	The cerebellopontine angle area ratio, disease duration, and type of offending vessel were identified as risk factors for recurrence

Smoking status: eX-smoker/eXposure to smoking (X)

When correlating the smoking status with different variables in our study population (Table 3), statistically significant conclusions were drawn. When associating it with age, we concluded a median age of 48.5 years in ever-smokers versus 60.0 years in never-smokers (p=0.0167). This concludes that in our cohort, smokers are significantly younger than non-smokers, thus the groups have different ages. The same analysis, but including 3 smoking categories, was conducted. The conclusion was that non-smokers were older and smokers (former/current) were younger (p=0.0479). The median age was 60.0 years in never-smokers, 49.5 years in current smokers, and 48.5 years in former smokers. The analysis is almost similar to the aforementioned one; however, this one is more detailed.

When associating smoking status with diagnosis, we found that HFS is a more frequent diagnosis in smokers than in non-smokers (p=0.0208, OR 18.53). The association is significant with a high OR, but the CI is very large. This is due to the fact that there are only 4 patients with HFS in the study group; thus, the OR is unstable, and the estimates might be imprecise.

When testing the same analysis but including 3 smoking categories (never/former/current), we found that in the TN group, 17 patients never smoked and 8 are currently smoking, while in the HFS group, 2 patients were former smokers and 2 are current smokers. This means that in our cohort, HFS is more common in smokers (former/current), while the TN group has an important never-smokers component (p=0.0019).

Another statistical analysis regarding the smoking status correlated the ever-smoker versus never-smoker with diagnosis, but adjusted for age and sex (OR=3.25; bootstrap 95% CI 1.58-6.05). This analysis was conducted in order to find out if the association between smoking status and diagnosis is still relevant after considering patients' age and sex. The adjusted OR is 3.25, and the bootstrap CI does not include 1, so the result is significant. Thus, even after adjustment for age and sex, the ever-smoking group is associated with a higher probability of HFS (versus TN) in our cohort. The limitation lies in the small number of patients with HFS (4 patients with reported smoking status), therefore the result could be interpreted more as exploratory. All of these analyses gave two conclusions: (1) in our cohort, smokers are younger, and (2) smoking is more associated with HFS diagnosis.

The medical literature exploring the relationship between smoking and NVCS reported various results, which may appear inconsistent; however, in the majority of the cases, the cohorts were larger. For example, in 2025, Shepherd et al. studied the correlations between tobacco use and TN and found that smoking is associated with a younger age of TN onset, more widespread facial pain, and worse long-term outcomes, suggesting that smoking may not only aggravate TN but also lead to poorer postoperative results [33].

In a more detailed approach, Miyazaki et al. found that smoking can reduce cortical responses to pain stimuli and that nicotine has a central analgesic effect on pain processing in the brain, but the effects were reported as short-term. However, this may explain why smokers sometimes can report lower pain perception and why nicotine dependence may be linked to pain modulation [34]. In contrast with these results, Holle et al. reported that the effects of nicotine are more complex, stimulating nicotinic acetylcholine receptors and modifying the excitability of neurons in the trigeminal subnucleus caudalis, thereby producing inhibition in the brainstem and facilitating pain processing in the cortex or thalamus [35].

In our study, results regarding the correlations between smoking and outcomes and complications were not statistically significant, which is also consistent with the results reported by Liu et al. [36]. The authors included 33 patients (13.3.%) who were smokers and found no significant association between smoking and postoperative complications in HFS patients. Furthermore, smoking did not significantly increase or decrease the risk of complications after MVD for HFS [36].

The total number of patients operated by endoscope assisted-MVD is 19, of which 14 had a reported smoking status. Seven patients never smoked before, while 7 patients were in the ever-smoking group (former or current). In 5 patients, there was no reported smoking status. In the QEVO derivation cohort with reported smoking status, the high-impact event results were 2/7 in the never-smoking group and 1/7 in the former/current smoking group. However, the Fisher p was 1.000, thus the results were not statistically significant. This concludes that smoking is not a predictor of a high-impact yield in our pilot derivation cohort.

Associated comorbidities (A)

Regarding the associated comorbidities in our cohort derivation, in 1 out of 4 patients without comorbidities, a high-impact endoscopic yield was reported (25%), while in 2 out of 15 patients with associated comorbidities, a high-impact yield was reported (13.3%). The Fisher's exact p-value is not statistically significant ($p=0.530$), therefore, the difference between 1/4 and 2/15 is not enough to consider that it was not random, especially in such a small sample size. The OR is 0.5 (95% CI 0.03-6.93), which is less than 1, suggesting a tendency to associate the comorbidities with less high-impact yield. However, CI>1 suggests a very imprecise result, due to the very small N. In conclusion, there is no proof that comorbidities may predict high-impact yield in our pilot study.

When comparing the age distribution in patients with comorbidities versus those without comorbidities, we concluded that age was significantly associated with the presence of comorbidities (Spearman $\rho=0.578$, $p=0.010$). Furthermore, patients with comorbidities were older than those without (Mann-Whitney $p=0.016$), and this collinearity supports a parsimonious approach for score derivation.

The medical literature reports many comorbidities as predictive factors in postoperative outcomes, and a summary of the results is presented in Table 5.

Table 5. A summary of studies that evaluate the clinical and prognostic relevance of comorbidities in TN and HFS.

Study	Type of NVCS	Comorbidity	Findings and clinical relevance	Predictive or prognostic implication
Shoraka et al., 2025 [37]	TN	Depression	Depression was associated with earlier pain recurrence after surgical treatment	Depression may predict shorter pain-free survival after surgery
Kalluri et al., 2025 [38]	TN	Depression	Depression was associated with greater postoperative pain and higher risk of pain recurrence	Depression may be a negative prognostic factor for postoperative outcome after MVD
Kalluri AL et al., 2023 [39]	TN	Concomitant autoimmune disease	Patients with autoimmune disease were more likely to have type 2 TN, worse postoperative BNI pain scores, and more frequent recurrent pain after MVD	Autoimmune comorbidity may indicate less favorable postoperative pain outcomes
Min L et al., 2020 [40]	HFS	Hypertension and diabetes mellitus	Diabetes affected abnormal muscle response related findings, while hypertension was linked to postoperative hearing-related risk	The reported comorbidities may modify intraoperative predictive markers and postoperative risk
Tian S et al., 2024 [41]	HFS	Hypertension	Hypertension was identified as an independent risk factor for poorer short-term outcome after botulinum toxin type A treatment	Hypertension may predict less favorable short-term response to botulinum toxin type A treatment
Wu F et al., 2021 [42]	HFS	Preoperative anxiety and depression	Anxiety and depression were associated with disease burden and postoperative outcome in adolescent HFS patients treated with MVD	Psychiatric comorbidity may influence symptom severity and surgical outcome
Cote DJ et al., 2019 [43]	TN/HFS	General comorbidity burden, including diabetes; ASA status	In a national MVD cohort, higher ASA class and certain comorbidities, including diabetes, were associated with adverse events and readmission	Comorbidity burden may predict perioperative complications after MVD

4.3. Alexa-Y: Score Construction and Performance

The Y in the ALEXA-Y score is the endpoint, which is defined as high-impact endoscopic yield (Y=1 if there is a strategy change and/or a hidden offender, otherwise Y=0). The incidence of high-impact cases in our study was concluded to be of 15.8% in 3 out of 19 cases. A strategy change was reported in 3 cases, confirmation-only in 16 cases, and a hidden offender in 0 cases.

The other candidate domains were A, L, E, X, and A. The ALEXA-Y Score was designed based on factors that were clinically easy to obtain, and that could contribute to or influence the probability that the endoscopy could be of high-impact. The domains were selected a priori based on clinical experience and medical literature: A - age, L - length of symptoms, E - timing of endoscopy, X - smoking, and A - associated comorbidities. The Y stands for endoscopic yield, which is the endpoint. However, given the limited number of high-impact cases, the model should remain parsimonious in order to avoid overfitting.

The current study evaluated every candidate domain through univariate comparisons (high-impact versus non-high-impact) and predictive utility (ROC/AUC). In our pilot study, age did not discriminate well (AUC almost 0.5, with a p-value that was not statistically significant), smoking status was not associated with high-impact yield, comorbidities did not predict high-impact yield, and were associated with age (collinearity), and the timing had a suggestive distribution, but not a significant one for high-impact (small N). Nevertheless, the duration of the symptoms showed the strongest results, with a tendency in group comparison and a good AUC.

When constructing the final score, we chose a simple rule based on symptom duration because it showed a predictive signal, and, from a clinical point of view, it is easy to apply. The threshold of 24 months (2 years) was selected as a data-driven threshold (it separates the groups very well), but it is also very easy to interpret. A score of 1 point was attributed if the duration of symptoms was less than or equal to 24 months, while a score of 0 points was attributed if the symptoms duration was greater than 24 months. A higher score suggests a higher probability of high-impact endoscopic yield.

Regarding the score performance, a score of 1 point was attributed to 3 out of 6 patients (high-impact in 50%), Fisher p=0.021, AUC for symptoms duration 0.854 with bootstrap 95% CI 0.667-1.000. The score separates a group with a very small probability of high-impact from a group with a high probability of high-impact yield.

We emphasize the fact that the current score is a pilot derivation and needs an external validation. The main limitation regards that our CIs are large due to the small N size and the small number of events. Table 6 summarizes the ALEXA Score.

Table 6. Prespecified candidate domains of the proposed ALEXA-Y framework and provisional pilot-derived implementation.

Component	**Meaning**	**Coding/threshold**	**Point**
A	Age	≥60 years	1
L	Length of symptoms	≤24 months	1
E	Endoscopy timing	Exploration AND final inspection	1
X	eX-smoker/smoking eXposure	Ever-smoker (current/former)	1
A	Associated comorbidities	Any comorbidity	1
Y	Yield (endpoint)	High-impact yield=strategy change and/or hidden offender	Outcome

In the present pilot derivation cohort (N=19, 3 events), the parsimonious final model retained the L component only, and the remaining domains are proposed as candidate components for evaluation in larger external validation cohorts. It is very possible that the other domains (A, E, X, A) could be relevant in bigger cohorts, but in our cohort could not be demonstrated as stable predictors.

5. Conclusions

To our knowledge, to date, there is no existing tool that can assess whether the endoscopy can have a high-impact in MVD for NVCS or not. Candidate domains were A-L-E-X-A, but the final parsimonious pilot score retained only the L component due to the limited number of high-impact events. Given the limited sample size, the ALEXA-Y score should be considered a derivation model requiring external validation on larger cohorts, and this is thoroughly encouraged.

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