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Surgical infarct volume reduction and functional outcomes in patients with ischemic cerebellar stroke: results from a multicentric retrospective study

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OBJECTIVE Recent work on ischemic cerebellar stroke has suggested that the resection of infarcted tissue may lead to improved functional outcomes compared with decompressive surgery alone. Nonetheless, no studies have assessed the extent to which necrotic tissue should be resected or if there are any volumetric thresholds capable of predicting functional outcomes in this patient population. In this study, the authors aimed to determine potential thresholds for volume reduction in ischemic cerebellar stroke in an effort to optimize the management of ischemic cerebellar stroke and, in so doing, improve functional outcomes.

METHODS This study is a multicentric retrospective study of patients who underwent surgery for the management of ischemic cerebellar stroke. Volumetric analyses of infarcted tissue present on CT scans were performed before and after surgical intervention(s). The final infarct volume (FIV) was computed as a percentage of the initial infarct volume (postoperative infarct volume/preoperative infarct volume × 100). The primary endpoint was functional outcome at 3 months, as determined by the modified Rankin Scale (mRS) score; mRS scores 0–2 were considered as favorable and mRS scores 3–6 as unfavorable. Receiver operating characteristic curves were used to explore the relationship between postoperative infarct volumes and FIV versus mRS score, and Youden's index was used to estimate potential volumetric thresholds.

RESULTS A total of 91 patients were included in the study. The mean pre- and postoperative infarct volumes were 45.25 (SD 18.32) cm^3 and 29.56 (SD 26.61) cm^3, respectively. Patients undergoing necrosectomy, regardless of whether via craniotomy or craniectomy, were more likely to have a favorable outcome at discharge (OR 16.62, 95% CI 2.12–130.33; $p = 0.008$) and at 3 months (OR 24.12, 95% CI 3.03–192.18; $p = 0.003$) postoperatively. Postoperative infarct volumes ≤ 17 cm^3 yielded a sensitivity of 77% and a specificity of 68% with regard to the prediction of favorable outcome at 3 months. The resection ≥ 50% of infarcted tissue was also predictive of favorable outcomes at 3 months (OR 7.7, 95% CI 2.7–21.8; $p < 0.001$).

CONCLUSIONS The reduction of necrotic tissue volumes by at least 50% and/or the reduction of the infarct volume by ≤ 17 cm^3 appear to be associated with favorable outcomes in patients with surgically managed ischemic cerebellar strokes.

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KEYWORDS cerebellum; ischemic stroke; strokectomy; craniectomy; surgery; vascular disorders

ABBREVIATIONS AUC = area under the curve; EVD = external ventricular drain; FIV = final infarct volume; GCS = Glasgow Coma Scale; mRS = modified Rankin Scale; NIHSS = National Institutes for Health Stroke Scale; ROC = receiver operating characteristic; SSI = surgical site infection.

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The lifesaving role of decompressive surgery in malignant middle cerebral artery stroke has been established through randomized controlled trials.[1] Nonetheless, the evidence supporting decompressive surgery as a treatment for ischemic stroke in the posterior fossa is less robust and comprises only small retrospective case series.[2] Importantly, recent studies have suggested that the resection of infarcted tissue in ischemic cerebellar stroke may yield superior functional outcomes.[3–6]

In the supratentorial compartment, stroke volumes > 270 cm^3 have been shown to be associated with unfavorable outcomes.[7] Additionally, pooled analyses from endovascular trials on recanalization of anterior circulation strokes have shown that an increase of infarct volume at follow-up is predictive of functional outcome.[8] Our group has demonstrated that infarct volumes > 35 cm^3 are predictive of unfavorable outcome, supporting surgical management in the posterior fossa.[6,9] However, no studies have assessed the role of surgical volume reduction with regard to functional outcomes in patients with ischemic cerebellar stroke.

Accordingly, herein we sought to determine potential thresholds for volume reduction in ischemic cerebellar stroke in an effort to optimize the management of ischemic cerebellar stroke and, in so doing, improve functional outcomes.

Methods

We conducted a retrospective multicenter study of patients undergoing surgery for the treatment of space-occupying ischemic cerebellar stroke between 2011 and 2021. The study was carried out in accordance with the Helsinki Declaration and with approval from the institutional review boards of the participating clinical centers. The requirement for informed consent was waived given the retrospective nature of the study.

Patients

All patients were treated and monitored in certified academic stroke units, in accordance with German national standards. Multimodal, interdisciplinary, complex stroke care was initiated in all patients. We included adult patients aged 18 years or older treated surgically for ischemic cerebellar stroke. Surgical indications and technique were carried out according to each institution's standards. Patients were stratified according to the surgical technique used: 1) craniotomy with infarct resection/necrosectomy, 2) craniectomy with infarct resection/necrosectomy, or 3) purely decompressive craniectomy without infarct resection. Only patients with full data sets were included in this study. Exclusion criteria were 1) concurrent stroke in extracerebellar regions, 2) radiologically inapparent stroke, and 3) insufficient clinical or radiological data.

Demographic and clinical parameters were collected and included the following: sex, age, and Glasgow Coma Scale (GCS) and National Institutes for Health Stroke Scale (NIHSS) scores at presentation. Comorbidities such as arterial hypertension, diabetes mellitus, chronic obstructive pulmonary disease and/or asthma, coronary artery disease, atrial fibrillation, and past medical history for stroke were also documented. Data on time from ictus to surgery were extracted as well. The length of hospitalization and postoperative complications, such as pneumonia, urinary tract infection, hemorrhagic transformation (defined as hemorrhage within the infarcted tissue after surgery), surgical site infection (SSI), and CSF leak/fistula, were also assessed.

Radiographic Parameters

Volumetric analysis of infarcted tissue on noncontrast CT scans was performed before and after surgical intervention. Infarct volume was calculated utilizing the automated volumetric region-of-interest function using Brainlab software (Brainlab AG). The final infarct volume (FIV), i.e., the infarct volume postoperatively, was computed as a percentage of the initial infarct volume (postoperative infarct volume/preoperative infarct volume × 100).

Primary and Secondary Endpoints

The primary endpoint of this study was functional outcome at 3 months, as determined by the modified Rankin Scale (mRS) score. Functional outcome was dichotomized as favorable (mRS scores of 0–2) and unfavorable (mRS scores of 3–6). The secondary outcome assessed was mortality at 3 months.

Statistical Analysis

Mean (SD) was used to report normally distributed continuous variables. Frequency and percentage were used to report categorical and ordinal variables. Receiver operating characteristic (ROC) curves were calculated for postoperative infarct volumes and FIV, for both mortality and dichotomized outcomes at 3 months per the mRS score. A p value < 0.05 was deemed statistically significant. Youden's index was used to determine the best cutoff values for FIV and postoperative infarct volumes for the prediction of mortality and functional outcome. Based on the calculated cutoff values for both parameters, an analysis of n × 2 contingency tables (chi-square test) was performed. Other variables that could affect outcome were also assessed in the same fashion. Results are reported using odds ratios and 95% confidence intervals. All statistical analyses were performed using IBM SPSS version 25 (IBM Corp.). Figures were created with Visme.

Results

In total, 91 patients with ischemic cerebellar stroke underwent surgery as part of the management. Patient recruitment by each center and the surgical technique used are illustrated in Supplementary Fig. 1. The mean age of patients was 65 (SD 13) years, and 42 patients (46.2%) were female. The mean GCS and NIHSS scores at admission were 10 (SD 5.1) and 10 (SD 12.2), respectively. Of 91 patients, 49 patients (53.8%) underwent craniotomy with necrosectomy, whereas 42 patients (46.2%) underwent craniectomy with or without necrosectomy. Pneumonia was the most frequent complication in the postoperative course (Table 1).

The groups stratified by different surgical technique were overall well balanced without significant difference regarding age, clinical admission status, preoperative infarct volume, and brainstem involvement. Time to surgical treatment, incidence of SSI, and frequency of external ventricular drain (EVD) use were among the variables that did show a significant difference between the groups. Details are illustrated in Table 2.

Predictors for Functional Outcome

In a univariate analysis of all parameters collected, surgical technique was significantly associated with functional outcome at discharge and 3 months. Patients undergoing infarct resection, regardless of whether via craniotomy or craniectomy, were more likely to have a favorable functional outcome at discharge (OR 16.62, 95% CI 2.12–130.33; $p = 0.008$) and at 3 months postoperatively (OR 24.12, 95% CI 3.03–192.18; $p = 0.003$). Brainstem involvement was predictive of functional outcome at discharge (OR 0.23, 95% CI 0.04–1.08; $p = 0.047$) and 3 months (OR 0.22, 95% CI 0.06–0.85; $p = 0.029$) as well. Postoperative pneumonia was associated with unfavorable functional outcome at discharge (OR 0.33, 95% CI 0.13–0.86; $p = 0.024$), but at 3 months this was no longer statistically significant.

Volumetric Analysis and Endpoints

The mean preoperative infarct volume was 45.25 (SD 18.32) cm^3, while the mean postoperative infarct volume was 29.56 (SD 26.61) cm^3. In the ROC curve analysis, postoperative infarct volumes ≤ 17 cm^3 had a sensitivity of 77% and a specificity of 68% with regard to the prediction of favorable outcomes at 3 months (Fig. 1A). Postoperative infarct volume, however, was not a good predictor of mortality (area under the curve [AUC] 0.540, $p = 0.611$). As illustrated in Fig. 1B, postoperative infarct volumes ≤ 17 cm^3 were also associated with improved rates of favorable outcomes at 3 months (OR 6.8, 95% CI 2.5–18.5; $p = 0.003$).

The mean FIV was 68.68% (SD 65.63%). This reduction in infarct volume was statistically significant ($p < 0.001$). In the ROC curve analysis, an FIV < 52% had a sensitivity of 74% and a specificity of 80% with regard to the prediction of favorable outcome at 3 months (AUC 0.753, $p < 0.001$) (Fig. 2A). However, mortality at 3 months could not be predicted using this cutoff value (AUC 0.492, $p = 0.919$). Among patients with ≥ 50% resection of infarcted tissue, 64% achieved favorable outcomes at 3 months as compared with 19% of patients with < 50% resection of infarcted tissue (OR 7.7, 95% CI 2.7–21.8; $p < 0.001$) (Fig. 2B).

Discussion

Resection of infarcted brain tissue secondary to ischemic stroke is not a well-established surgical strategy, yet small case series have suggested that performing resection of such tissue in addition to or instead of decompressive craniectomy may lead to better functional outcomes.[10–12] A small randomized controlled trial also suggested that stereotactic aspiration of infarcted tissue may lead to favorable outcomes compared with decompressive craniectomy.[13] Consistent with such literature, there are a number of recent case series supporting the benefit of resection for infarcted tissue in cerebellar stroke as well.[3–5] Despite such work, the extent to which necrotic tissue should be resected has not yet been established.

This is the first study to quantitatively evaluate the influence of surgical infarct volume reduction on functional outcomes in ischemic stroke (i.e., in the cerebrum or cerebellum). Previous volumetric work in stroke has focused on futility analyses in an effort to better select patients for endovascular treatment and/or predict outcomes in the setting of anterior circulation strokes.[14,15] Consistent with the aforementioned evidence/literature and as described above, data on the evaluation of ischemia secondary to posterior circulation insults remain limited. As such, we feel that this information would be valuable when surgically managing cerebellar stroke, as it can help better define the goals of the operation.

According to our results, the reduction of ischemic tissue volumes to ≤ 17 cm^3 or at least approximately 50% of the preoperative infarct volume appears to be associated with improved functional outcomes. The pathophysiologi-

TABLE 1. Clinical parameters, interventions, and postoperative course of the entire cohort undergoing surgery for space-occupying cerebellar stroke

	Value
Clinical parameters	
Age, yrs, mean (SD)	65 (13.0)
Sex, M/F	49 (53.8)/42 (46.2)
Arterial hypertension	79 (86.8)
Diabetes mellitus type 2	27 (29.7)
COPD/asthma	12 (13.2)
Coronary artery disease	18 (19.8)
Atrial fibrillation	24 (26.4)
Past medical history of stroke	13 (14.3)
Prior use of antiplatelet agents	31 (34.1)
GCS score at admission, mean (SD)	10 (5.1)
NIHSS score at admission, mean (SD)	10 (12.2)
Brainstem infarction	17 (18.7)
Interventions	
IV thrombolysis	17 (18.7)
Mechanical thrombectomy	12 (13.2)
Time to surgery after ictus, hrs, mean (SD)	22 (30.2)
Craniotomy/craniectomy	49 (53.8)/42 (46.2)
Postoperative course	
Pneumonia	42 (46.2)
UTI	11 (12.1)
Hemorrhagic transformation postoperatively	4 (4.4)
SSI	23 (25.3)
CSF fistula	3 (3.3)
Length of hospitalization, days, mean (SD)	19 (12.7)

COPD = chronic obstructive pulmonary disease; IV = intravenous; UTI = urinary tract infection.
Values are presented as number of patients (%) unless otherwise indicated.

TABLE 2. Clinical and radiological parameters, treatment, complications, and clinical outcomes of patients undergoing surgery for space-occupying cerebellar infarction, stratified by surgical technique

	Suboccipital Craniotomy w/ Necrosectomy	Suboccipital Craniectomy w/ Partial Necrosectomy	Suboccipital Craniectomy w/o Necrosectomy	p Value
Total no. of patients	49 (53.8)	18 (19.8)	24 (26.4)	
Clinical characteristics				
GCS score prior to surgery, mean (SD)	10 (5.1)	10 (5.3)	10 (4.9)	0.908
NIHSS score at admission, mean (SD)	6 (7.6)	8 (8.9)	13 (15.4)	0.591
Time from ictus to surgery, hrs, mean (SD)	16 (28.0)	14 (22.9)	36 (27.0)	**0.024**
Radiological parameters				
Infarct vol, cm^3, mean (SD)	47 (18.2)	42 (18.1)	45 (19.1)	0.867
Brainstem infarction	12 (24.5)	2 (11.1)	3 (12.5)	0.306
Interventions				
Thrombolysis	9 (18.4)	2 (11.1)	6 (25.0)	0.519
Mechanical recanalization	6 (12.2)	2 (11.1)	4 (16.7)	0.835
Additional use of EVD	2 (4.1)	14 (77.8)	22 (91.7)	**<0.001**
Complications				
Pneumonia	19 (38.8)	12 (66.7)	11 (45.8)	0.127
UTI	8 (16.3)	1 (5.6)	2 (8.3)	0.393
Hemorrhagic transformation	1 (2.0)	1 (5.6)	2 (8.3)	0.367
SSI	11 (22.4)	10 (55.6)	2 (8.3)	**0.034**
CSF leak	1 (2.0)	0 (0)	1 (4.2)	0.376
Outcome				
Length of hospitalization, days, mean (SD)	20 (13.7)	21 (10.1)	15 (9.4)	0.437
mRS score 0–2 at discharge	21 (42.9)	6 (33.3)	1 (4.2)	**0.003**
mRS score 0–2 at 3 mos	25 (51.0)	8 (44.4)	1 (4.2)	**0.001**
Mortality at discharge	13 (26.5)	1 (5.6)	3 (12.5)	0.099

Values are presented as number of patients (%) unless otherwise indicated. Boldface type indicates statistical significance.

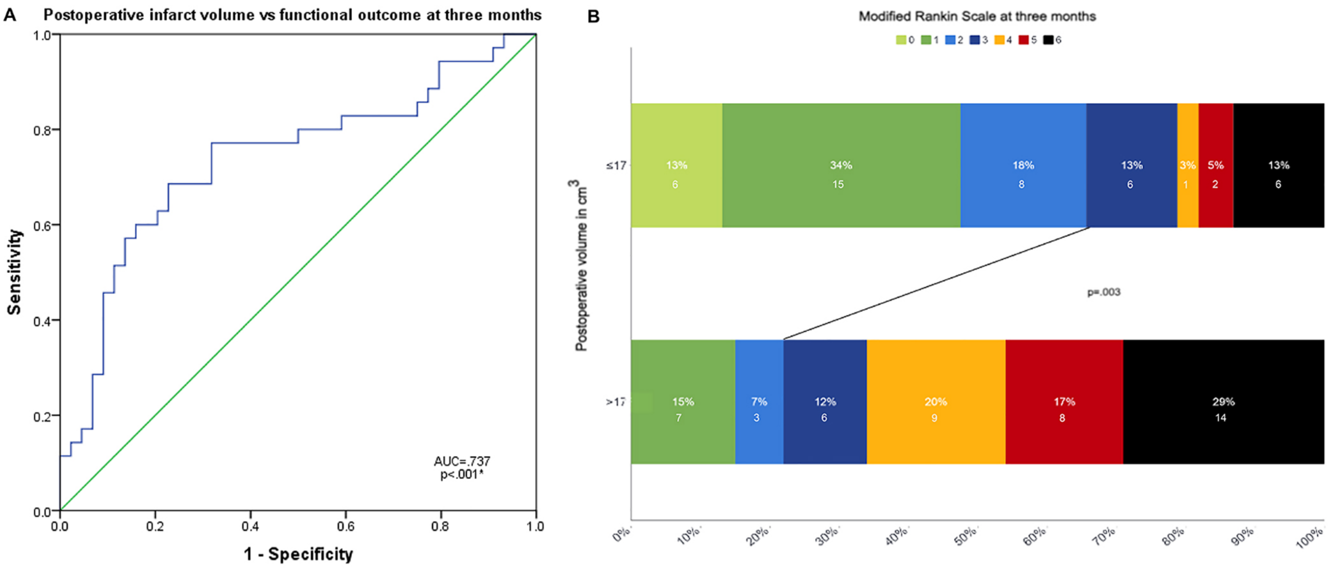

FIG. 1. A: ROC curve of postoperative infarct volume and dichotomized functional outcome at 3 months, according to the mRS score. The *asterisk* denotes statistical significance. **B:** Patients stratified according to postoperative infarct volume and functional outcome at 3 months, according to the mRS score. A postoperative infarct volume ≤ 17 cm^3 was predictive of a favorable functional outcome (OR 6.8, 95% CI 2.5–18.5; p = 0.003). Figure is available in color online only.

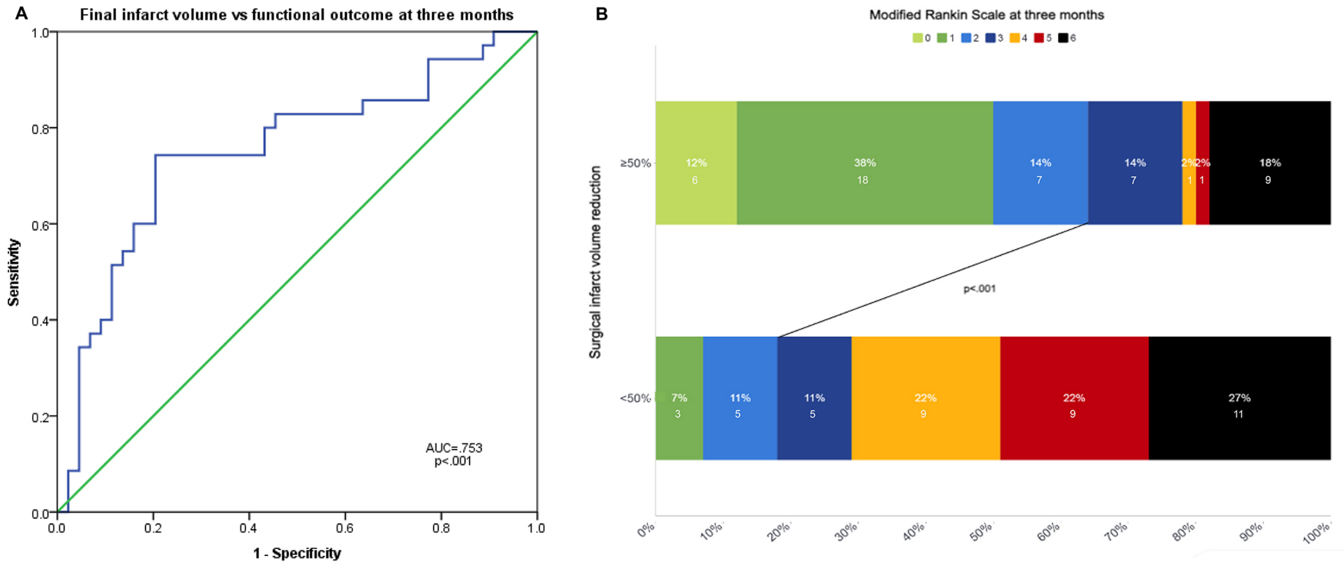

FIG. 2. **A:** ROC curve of FIV and dichotomized functional outcome at 3 months, according to the mRS score. **B:** Patients stratified by surgical volume reduction of infarcted tissue and functional outcome at 3 months, according to the mRS score. A postoperative volume reduction ≥ 50% was predictive of favorable functional outcome (OR 7.7, 95% CI 2.7–21.8; p < 0.001). Figure is available in color online only.

cal mechanisms underlying these treatment effects remain speculative and cannot be fully elucidated by our study because of its design. We postulate that resection of the infarcted tissue has an effect beyond the purely mechanistic decompression of the posterior fossa. Through the infarcted tissue, cytotoxic edema ensues, which triggers a maladaptive inflammatory cascade with activation of the microglia, the complement system, and breakdown of the blood-brain barrier. By removing the initial insult, these pathophysiological mechanisms might be interrupted, thus in part explaining the improvements in outcome at 3 months.[16,17]

Limitations and Future Directions

The main limitation of this study is its retrospective design, which renders it subject to selection bias. Patients were not randomized to undergo a specific surgical technique, and therefore the amount of infarcted tissue resected was left to the attending surgeon's discretion and subject to a myriad of uncontrolled clinical and surgical circumstances. The fact that surgery was not performed in a standardized fashion also renders our results less reliable. Factors that could affect outcome, such as visualization of the fourth ventricle and opening of the basal cisterns to alleviate hydrocephalus, were not assessed and/or further evaluated. In this regard, it is also noteworthy that patients who underwent craniectomies, irrespective of additional necrosectomy, received EVDs at a significantly higher rate. This could be because of persistent hydrocephalus, which, in turn, might have affected outcome. Additionally, patients who did not undergo infarct resection were surgically treated significantly later during the course of the disease; this might have negatively impacted their outcome as well. Nevertheless, this study provides a basis on which to build.

It is also prudent to note that the infarction volumes reported in our study were derived from non–contrast-enhanced CT scans, and as such, discrimination between infarcted tissue and edema, both pre- and postoperatively, may have been suboptimal.[18] While diffusion-weighted MRI offers more precise information on cerebellar infarction, it is not widely available and is not routinely performed in the acute evaluation of posterior fossa strokes. Future work may therefore seek to use CT perfusion imaging.

Another potential drawback of this study is the assessment of functional outcome with the mRS alone. While this scale is commonly used to report outcome in ischemic stroke, it may underrepresent deficits in patients with cerebellar pathology. Dedicated clinical scales, such as the modified International Cooperative Ataxia Rating Scale and the Brief Ataxia Rating Scale, have been shown to be more sensitive in assessing patients' neurological impairment in cerebellar pathology.[19,20] Unfortunately, given the retrospective nature of the analysis and the incomplete documentation in patients' records, this limitation cannot be overcome.

This study is a part of a multicentric effort to better understand the surgical aspects of ischemic cerebellar stroke management and constitutes a first step in providing evidence to guide operative decision-making and strategy. Future studies should seek to include the molecular and histopathological analyses of inflammatory parameters in the surrounding parenchyma in an effort to fully elucidate the mechanism underlying the benefits of necrosectomy.

Conclusions

Our results suggest that a reduction of at least 50% of noted infarct volumes or a reduction of necrotic tissue ≤

17 cm^3 might be associated with favorable functional outcomes at 3 months postoperatively in patients with ischemic cerebellar stroke.

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Disclosures

Dr. Bernstock reported an equity position in Treovir Inc. and UpFront Diagnostics; being a co-founder of Centile Bioscience; and being on the scientific advisory board of NeuroX1 and QV Bioelectronics. Dr. Mielke reported consulting fees from Medtronic outside the submitted work. Dr. Schaefer reported nonfinancial support from Bayer AG outside the submitted work. Dr. Gessler reported personal fees from Aesculap, Signus, and AstraZeneca outside the submitted work.

Author Contributions

Conception and design: Hernandez-Duran, Bernstock, Dinc, Freiman, Konczalla, Won. Acquisition of data: Hernandez-Duran, Walter, Dinc, Dubinski, Mielke, Naser, Rohde, Senft, Schaefer, Won. Analysis and interpretation of data: Hernandez-Duran, Walter, Behmanesh, Dinc, Dubinski, Freiman, Konczalla, Mueller, Naser, Rohde, Won, Gessler. Drafting the article: Hernandez-Duran, Walter, Bernstock, Czabanka, Won. Critically revising the article: Walter, Bernstock, Czabanka, Dinc, Freiman, Konczalla, Mielke, Mueller, Naser, Rohde, Senft, Unterberg, Won, Gessler. Reviewed submitted version of manuscript: Walter, Bernstock, Czabanka, Dinc, Konczalla, Mielke, Senft, Unterberg, Won, Gessler. Approved the final version of the manuscript on behalf of all authors: Hernandez-Duran. Statistical analysis: Hernandez-Duran, Melkonian, Mueller. Administrative/technical/material support: Hernandez-Duran, Naser, Unterberg, Gessler. Study supervision: Hernandez-Duran, Freiman, Rohde, Unterberg, Won, Gessler.

Supplemental Information

Online-Only Content

Supplemental material is available with the online version of the article.

Supplementary Figure 1. https://thejns.org/doi/suppl/10.3171/2024.3.JNS232883.

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