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Necrosectomy Versus Stand-Alone Suboccipital Decompressive Craniectomy for the Management of Space-Occupying Cerebellar Infarctions—A Retrospective Multicenter Study

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BACKGROUND AND OBJECTIVES: Space-occupying cerebellar stroke (SOCS) when coupled with neurological deterioration represents a neurosurgical emergency. Although current evidence supports surgical intervention in such patients with SOCS and rapid neurological deterioration, the optimal surgical methods/techniques to be applied remain a matter of debate.

METHODS: We conducted a retrospective, multicenter study of patients undergoing surgery for SOCS. Patients were stratified according to the type of surgery as (1) suboccipital decompressive craniectomy (SDC) or (2) suboccipital craniotomy with concurrent necrosectomy. The primary end point examined was functional outcome using the modified Rankin Scale (mRS) at discharge and at 3 months (mRS 0-3 defined as favorable and mRS 4-6 as unfavorable outcome). Secondary end points included the analysis of in-house postoperative complications, mortality, and length of hospitalization.

RESULTS: Ninety-two patients were included in the final analysis: 49 underwent necrosectomy and 43 underwent SDC. Those with necrosectomy displayed significantly higher rate of favorable outcome at discharge as compared with those who underwent SDC alone: 65.3% vs 27.9%, respectively ($P < .001$, odds ratios 4.9, 95% CI 2.0-11.8). This difference was also observed at 3 months: 65.3% vs 41.7% ($P = .030$, odds ratios 2.7, 95% CI 1.1-6.7). No significant differences were observed in mortality and/or postoperative complications, such as hemorrhagic transformation, infection, and/or the development of cerebrospinal fluid leaks/fistulas.

CONCLUSION: In the setting of SOCS, patients treated with necrosectomy displayed better functional outcomes than those patients who underwent SDC alone. Ultimately, prospective, randomized studies will be needed to confirm this finding.

KEY WORDS: Ischemic stroke, Surgery

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ABBREVIATIONS: AF, atrial fibrillation; **AHT,** arterial hypertension; **CAD,** coronary artery disease; **DM,** diabetes mellitus; **EVD,** external ventricular drain; **NIHSS,** National Institutes for Health Stroke Scale; **SOCS,** space-occupying cerebellar infarction; **SDC,** suboccipital decompressive craniectomy; **SSI,** surgical site infection.

Ischemic stroke is one of the leading causes of disability and death worldwide. Although cerebellar stroke only constitutes approximately 3% of all ischemic strokes, events in this location can lead to rapid neurological deterioration and death if not timely recognized and treated aggressively.[1,2]

Space-occupying cerebellar stroke (SOCS) constitutes a neurosurgical emergency; this is easily explained by the anatomic constraints of the posterior fossa, which is not able to accommodate edematous/infarcted parenchyma secondary to ischemia or cerebellar bleeds.[3] Such insults can lead to the development of acute hydrocephalus by occlusion of the fourth ventricle, as well as to brainstem compression.[4]

Current evidence supports emergent surgical intervention in patients with SOCS and rapid neurological deterioration.[5] However, the surgical technique to be applied warrants further analysis, as the evolution of surgery for SOCS has been an interesting one. In 1956, Lindgren[6] and Fairburn and Oliver[7] described the first cases of surgical treatment for SOCS. Both studies discuss posterior fossa exploration, which presupposed a large craniectomy through which the cerebellum was widely exposed (ie, from the transverse sinus superiorly to the sigmoid sinus laterally and the foramen magnum caudally); dural closure was not performed, and careful muscle suturing was undertaken.[8] In addition to posterior fossa exploration, both aforementioned studies described the resection of infarcted tissue in an effort to relieve mass effect.

Since those initial reports, neurosurgery has advanced. Novel diagnostic tools and techniques have facilitated a litany of surgical approaches to the cerebellum that are relevant for SOCS albeit with small iterations and variations between procedures. Currently, the most used techniques are as follows: suboccipital decompressive craniectomy (SDC) and duraplasty (often with the placement of an external ventricular drainage [EVD])[9-17] and resection of the infarcted tissue alone, ie, necrosectomy,[18,19] SDC with necrosectomy,[9,10,12,15,16,19] or SDC with additional resection of the posterior arch of C1.[14,16] Thus, no standardized surgical strategy has been established, given that most of these studies are relatively small, uncontrolled case series.

Accordingly, herein we have attempted to elucidate whether a specific surgical technique may be associated with better functional outcomes in patients suffering from SOCS by comparing stand-alone SDC and suboccipital craniotomy with necrosectomy as treatment strategies in patients with ischemic cerebellar stroke.

METHODS

We conducted a retrospective, multicenter study of patients undergoing surgery for the treatment of SOCS at 5 tertiary centers in Germany between 2015 and 2019. Only patients with ischemic strokes were included; hemorrhagic cerebellar strokes and/or traumatic arterial dissections resulting in infarction were excluded. Owing to the retrospective nature of the analysis, the requirement for informed consent was waived. The study was carried out in accordance with the 1964 Declaration of Helsinki and with approval from the Internal Review Boards of the participating centers.

Patients

Demographic and clinical parameters were collected, including 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/asthma, coronary artery disease, atrial fibrillation, and positive medical history for stroke were also documented.

Surgical Strategy

Patients suffering from SOCS underwent surgery, in accordance with current guidelines.[5] Allotment to surgical procedure was at institution's discretion. For the purposes of this study, patients were then stratified according to the type of surgery they underwent as (1) pure SDC or (2) suboccipital craniotomy with necrosectomy, ie, resection of the infarcted tissue in the cerebellar hemispheres; in cases of brainstem involvement, resection of infarcted tissue herein was not pursued. The additional use of an EVD was at the discretion of the managing team. Patients treated with EVDs alone were not included in the analysis.

Radiographic Parameters

A volumetric analysis of infarcted tissue on computed tomography scan was performed before and after surgical intervention. Infarct volume was calculated using the ABC/2 formula, as described by Huttner et al.[20] In addition, brainstem involvement was evaluated.

Postoperative Management

All patients were monitored in certified stroke units, in accordance with German national standards. Multimodal, interdisciplinary, complex stroke care was initiated on all patients. By only recruiting patients treated at tertiary care centers, the authors attempted to reduce the risk of bias.

Primary and Secondary End Points

The primary end point of this study was functional outcome at discharge and at 3 months, as determined by the modified Rankin Scale (mRS). Functional outcome was dichotomized as favorable for mRS 0–3 and unfavorable for mRS 4–6.

Secondary end points were in-house postoperative complications, such as pneumonia, urinary tract infections, hemorrhagic transformation (defined as hemorrhage within the infarcted tissue after surgery), surgical site infections, or cerebrospinal fluid (CSF) leaks/fistulas; mortality; and length of hospitalization.

Statistical Analysis

Means (± SD) were used to report normally distributed continues variables. For continuous variables, 1-way analysis of variance was performed to elucidate differences between the 2 surgical strategies. Frequencies and percentages were used to report categorical and ordinal variables. Univariate statistical analysis was performed to identify

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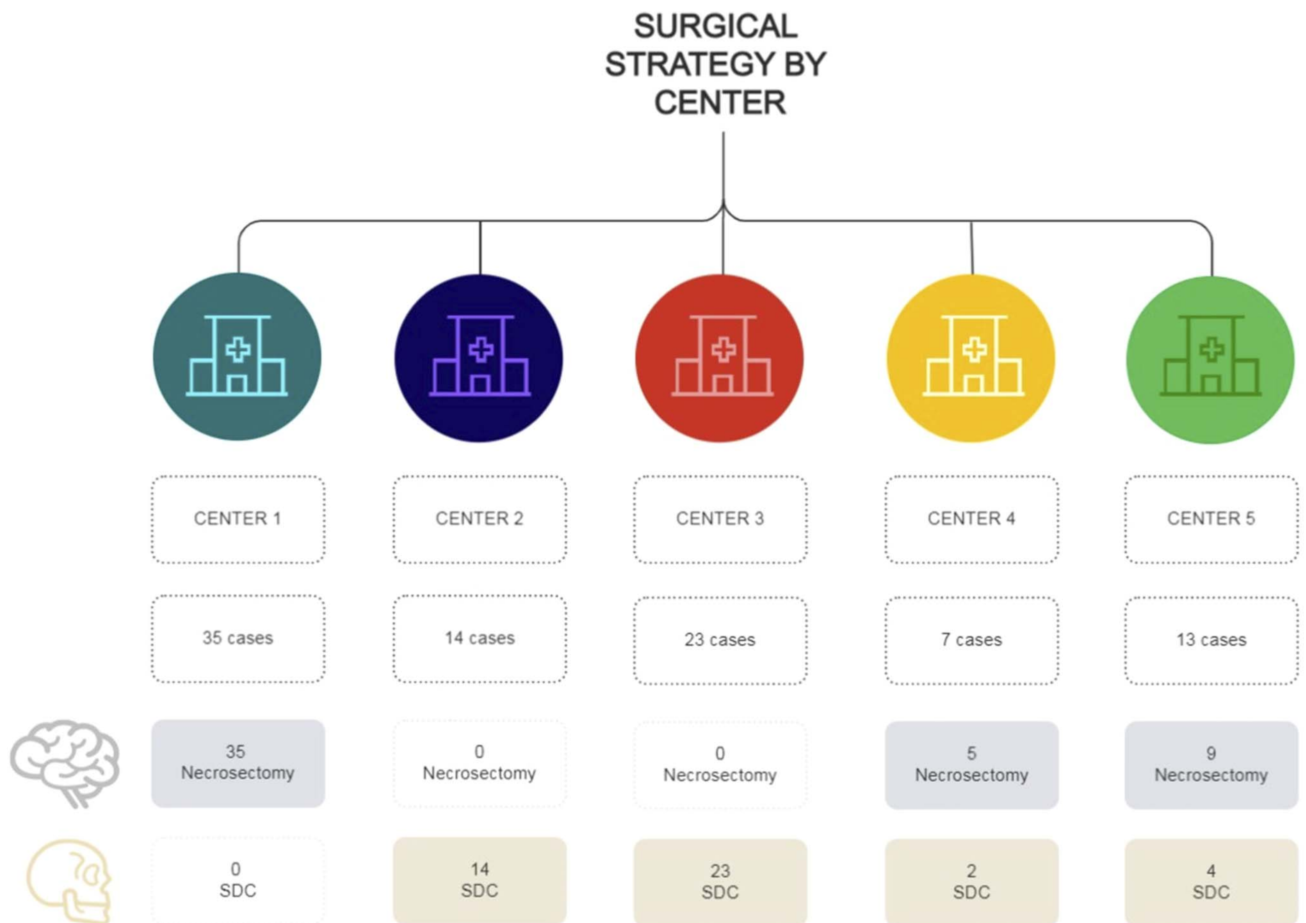

FIGURE 1. *Allotment of surgical strategies according to treating centers. SDC, suboccipital decompressive craniectomy.*

differences between patients undergoing SDC and necrosectomy: The χ^2 test (for analysis of N × 2 contingency tables) was performed for categorical and/or ordinal variables. The results are reported in odds ratios (OR) and 95% CI. Furthermore, a multivariate regression analysis was performed to assess which factors were associated with unfavorable outcome. Statistical significance was assumed at $P \leq .05$. Statistical analysis was performed with IBM® SPSS® v. 25 (IBM Corp). Figures were generated with Visme® (Easy WebContent, Inc.).

RESULTS

Of 131 identified patients with SOCS amenable to surgical therapy, 4 patients (3.1%) were excluded because they solely underwent placement of an EVD. 35 patients (26.7%) were excluded because of incomplete and/or compromised data sets. In total, 92 patients were included. Allotment of patients to the surgical technique is illustrated in Figure 1. Demographic data and comorbidities are summarized in Table 1.

Group Comparisons

As illustrated in Table 2, most patients underwent suboccipital craniotomy with necrosectomy (n = 49/92, 53%). Of note, none of the patients treated using SDC underwent additional necrosectomy; however, the majority of them also underwent placement of an EVD (n = 37/43, 86%). Contrarily, only a minority of patients treated with necrosectomy underwent EVD placement postoperatively because of persistent hydrocephalus (n = 2/49, 4.1%). No statistically significant difference was observed for medical (P = .977) or interventional treatment (P = .579) between both groups. Presenting GCS (P = .564) and NIHSS (P = .240) did not differ between both groups. Similarly, brainstem involvement was seen equally in both groups (P = .204). As expected, necrosectomy achieved a greater infarct volume reduction than SDC, which was statistically significant (P < .001). Notably, SDC was performed later than necrosectomy; this difference was statistically significant (P = .025). Conversely, length of hospitalization was comparable in both cohorts (P = .530).

TABLE 1. Demographic Data and Comorbidities of the Entire Cohort Undergoing Surgery for SOCS, Irrespective of Surgical Technique

Variable	n or mean	% or SD
Age, mean	65	12.9
Sex—male/female	50/42	54.3/45.7
AHT	80	87.0
DM type 2	28	30.4
COPD/asthma	12	13.0
CAD	18	19.6
AF	24	26.1
Medical history of stroke	13	14.1
Prior use of anticoagulants	18	19.6
Prior use of antiplatelet agents	31	33.7
GCS at admission, mean	10	5.1
NIHSS at admission, mean	10	11.2

AF, atrial fibrillation; AHT, arterial hypertension; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; GCS, Glasgow Coma Scale; NIHSS, National Institutes for Health Stroke Scale; SOCS, space-occupying cerebellar infarction.

Primary and Secondary End Points

As shown in Figure 2, functional outcomes at discharge and 3 months were statistically significantly better in the necrosectomy group: Those with necrosectomy had favorable outcome in 65.3% cases, whereas those with SDC had favorable outcome in 27.9% (P < .001, OR 4.9, 95% CI 2.0-11.8). This difference was also observable at 3 months: 65.3% of the necrosectomy patients vs 41.7% of the SDC patients, respectively (P = .030, OR 2.7, 95% CI 1.1-6.7).

Although mortality was higher in the necrosectomy group at 18.4% vs 7.0% in the SDC group, this difference did not reach statistical significance (P = .162). In 78% of deceased cases in the necrosectomy cohort, this was due to withdrawal of care.

For secondary outcomes, as shown in Table 2, no statistically significant differences were observed regarding hemorrhagic transformation (P = .494), surgical site infections (P = .279), and/or CSF leaks (P = .574). Of note, 1 patient had subtotal resection of the infarcted tissue and suffered hemorrhagic transformation. Patients undergoing SDC were shown to have more cases of postoperative pneumonia (P = .040). In the multivariate regression analysis, age (P = .040), GCS at admission (P = .006), brainstem involvement (P = .010), and surgical strategy (P < .001) were independent predictors for unfavorable outcomes.

DISCUSSION

To our knowledge, this study represents the largest series of patients undergoing surgery for SOCS. Our results suggest that necrosectomy using craniotomy yields better functional outcomes than SDC alone in the setting of SOCS. Contrary to malignant strokes of the anterior circulation, where decompressive surgery has been demonstrated to prevent mortality and reduce disability in randomized controlled trials,[21] purely decompressive surgery in the posterior fossa appears insufficient.

In a comparative study of patients undergoing EVD placement vs SDC with or without necrosectomy, Kudo et al[9] demonstrated that patients undergoing necrosectomy had more favorable functional outcomes than those treated with EVDs alone. Similarly, Kim et al,[12] Juttler et al,[16] Raco et al,[17] and Jauss et al[15] advocate for the addition of necrosectomy to SDC in severe SOCS cases in an effort to improve patient outcomes. These findings were corroborated in a systematic review and meta-analysis by Ayling et al,[22] where the addition of necrosectomy appeared to correlate with more favorable functional outcomes in SOCS. Furthermore, Hernández-Durán et al[18] and Tartara et al,[19] in 2 separate small case series, demonstrated equipoise between SDC and necrosectomy. Such findings must be confirmed by a randomized-controlled trial of surgical techniques for SOCS.

We hypothesize that the removal of necrotic tissue might interrupt the inflammatory cascade[23] that has been shown to ensue during ischemic stroke.[23] The blood-brain barrier is perturbed during ischemic stroke, and leukocytes invade the parenchyma, leading to increased cell death and cytotoxic edema.[24] This phenomenon might have contributed to the superior functional results observed in the necrosectomy group, but further studies are needed to corroborate these theoretical assumptions. Most patients undergoing SDC also had an EVD placed, whereas those with necrosectomy did not. We hypothesize that, by removing infarcted tissue, the occlusion of the fourth ventricle/CSF outflow can be relieved, thus reducing the need for an EVD or other forms of CSF diversion.[18] Prompt restoration of CSF flow dynamics may also have contributed to the observed differences noted in functional outcome. However, EVD placement has not been shown to influence survival and/or outcomes in the literature[9,13,15]; thus, this assumption needs to be corroborated in further studies.

Notably, we observed higher in-house mortality in the necrosectomy group. Although the difference did not reach statistical significance, it is alarming that mortality in the necrosectomy group almost doubled compared with those with SDC. It appears that necrosectomy produces dichotomized results for functional outcome. The reasons for this observed difference remain unclear because the predictors of unfavorable functional outcome (age, GCS at admission, and brainstem involvement) in our cohort were comparable in both groups. Studies conducted on elderly patients with stroke undergoing mechanical thrombectomy have yielded similarly dichotomized results, with relatively high mortality or good functional outcomes[25-27]: This was mostly due to withdrawal of care by relatives. In our study, 78% of deceased cases in the necrosectomy group were due to withdrawal of care. Unfortunately, factors contributing to this difference in mortality can only be estimated, and further studies will need to elucidate

TABLE 2. Clinical and Radiological Parameters, Treatment, Complications, and Clinical Outcomes of Patients Undergoing Surgery for Space-Occupying Cerebellar Infarction, Stratified by Surgical Technique

	Full cohort with surgery (n = 92)			
	Suboccipital craniotomy and necrosectomy	Suboccipital craniectomy	*P* value	OR (95% CI)
Total (%)	49 (53)	43 (47)	NA	NA
Clinical parameters				
GCS before surgery (SD)	10 (5.1)	11 (5.0)	.564	NA
NIHSS at admission (SD)	6 (7.6)	11 (13.1)	.240	NA
Time from ictus to surgery in hours (SD)	16 (28.0)	38 (62.8)	.025*	NA
Radiological parameters				
Infarct volume in mL, mean (SD)	47 (18.2)	44 (18.4)	457	NA
Postoperative infarct volume in mL, mean (SD)	16.5 (19.3)	44.8 (26.1)	<.001*	NA
Brainstem infarction (%)	12	6	.204	2.0 (0.7-5.9)
Medical and interventional treatment				
Thrombolysis (%)	9 (18.4)	8 (18.6)	.977	1.0 (0.3-2.8)
Mechanical recanalization (%)	6 (12.2)	7 (16.3)	.579	0.7 (0.2-2.3)
Additional use of EVD (%)	2 (4.1)	37 (86.0)	<.001*	144.9 (27.6-760.1)
Complications and hospitalization				
Pneumonia (%)	18 (36.7)	25 (58.1)	.040*	0.4 (0.2-1.0)
UTI (%)	9 (18.4)	2 (4.7)	.060	4.6 (0.9-22.7)
Hemorrhagic transformation (%)	1 (2.0)	2 (4.7)	.494	0.4 (0.1-4.9)
SSI (%)	11 (22.5)	14 (32.6)	.279	0.6 (0.2-1.5)
CSF leak (%)	1 (2.4)	0 (0)	.57	2.6 (0.1-66.3)
Length of hospitalization in days (SD)	19 (13.8)	17 (9.7)	.530	NA
Functional outcome				
At discharge (mRS 0-3) (%)	32 (65.3)	12 (27.9)	<.001*	4.9 (2.0-11.8)
At 3 months (mRS 0-3) (%)	32 (65.3)	15 (41.7)	<.030*	2.7 (1.1-6.7)
Mortality at discharge	9 (18.4))	3 (7.0)	.162	3.0 (0.8-11.9)

CSF, cerebrospinal fluid; EVD, external ventricular drain; mRS, modified Rankin Scale; NIHSS, National Institutes for Health Stroke Scale; OR, odds ratio; SSI, surgical site infection; UTI, urinary tract infection.
* denotes statistical significance

which patients might benefit from this surgical strategy and which ones might be more amenable for SDC or best supportive care.

We also found that patients subjected to SDC were operated on later than those undergoing necrosectomy. Owing to the retrospective nature of the analysis, we cannot fully elucidate the reasons behind these differences in surgical timing. We hypothesize that they are due to institutional standards and aggressiveness in indicating surgery because patients' preoperative clinical status did not differ among both cohorts. Additional work is required to establish the best time point for surgery in SOCS.

Furthermore, we identified differences in postoperative complications, with patients undergoing SDC having been shown to have an increased incidence of pneumonia. The higher incidence of pneumonia may have contributed to the difference in functional outcomes at discharge because stroke-associated pneumonia

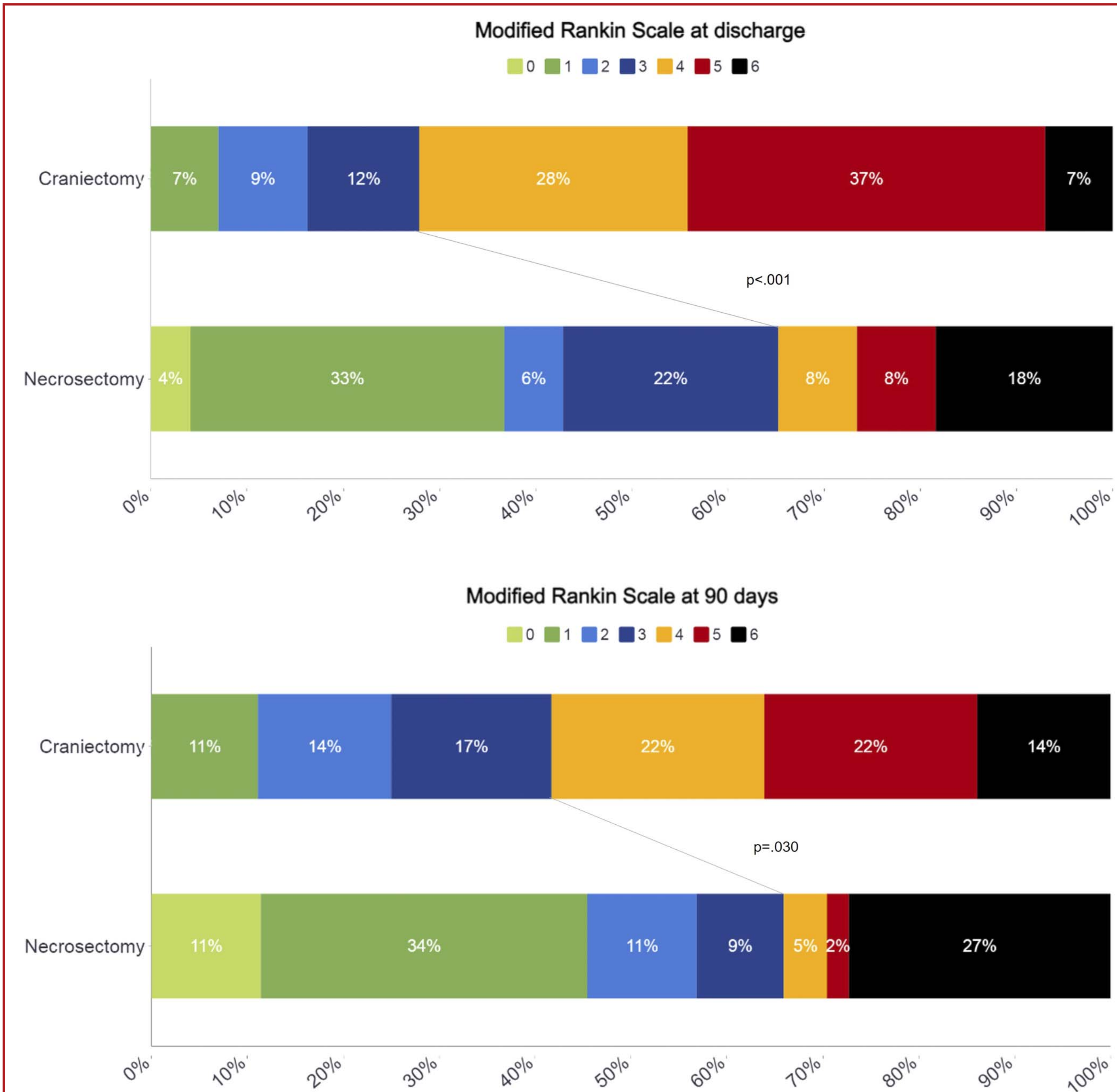

FIGURE 2. *Functional outcomes according to modified Rankin Scale of patients undergoing surgery for space-occupying cerebellar infarction, stratified by surgical technique at discharge and 3 months.*

has been shown in many studies to negatively affect functional outcome, prolong hospitalization, and increase mortality.[28-30] Nevertheless, pneumonia was not a significant predictor of outcome in the multivariate analysis, and length of hospitalization was comparable in both groups. Why in fact patients undergoing SDC developed pneumonia more often is unknown but may have been attributable to longer ventilation periods and/or a higher incidence of cranial nerve dysfunction; future work will be required to confirm such associations.

Limitations

Owing to the retrospective nature of the analysis, our study is by definition subject to a litany of biases. Choice of surgical strategies and techniques were left to surgeon's discretion and/or institutional protocols. Furthermore, we did not do a subgroup analysis of patients undergoing additional EVD placement. EVD placement was possibly heterogeneously indicated, either directly perioperatively or protractedly because of persistent hydrocephalus. This, in turn, did not allow us to account for the potential effects of persistent hydrocephalus on functional outcome and might have thus skewed the results.

Nevertheless, our study is the largest to date evaluating surgical strategies in SOCS. Importantly, all these patients underwent treatment at high-volume university hospitals in Germany, thus rendering them comparable with one another. Such work stands in stark contrast to previous meta-analyses and systematic reviews that examined patients treated in different eras/countries with varying technologies and protocols.

CONCLUSION

In the setting of SOCS, patients treated with suboccipital craniotomies/necrosectomy displayed better functional outcomes as compared with those who underwent SDC. Ultimately, prospective randomized studies will be needed to confirm such findings.

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COMMENTS

The authors reviewed a multi-institutional experience of posterior fossa strokes treated with either decompressive craniectomy or decompression as well as resection of infarcted tissue. This study found that more patients had a favorable modified Rankin Scale 3 months after necrosectomy compared with decompressive craniectomy alone. Unfortunately, there was also a higher rate of mortality, although this was associated with withdrawal of care.

This favorable finding occurred despite nearly twice as many patients having brainstem involvement in the group undergoing tissue resection. However, a key distinction may be the remarkably earlier surgery, nearly a day earlier in patients undergoing necrosectomy. This may suggest time-to-surgery as a key driver in outcomes. Differential time-to-surgery may also reflect workflow differences between the 5 centers, with 1 center enrolling 70% of the patients with necrosectomy while not performing any craniectomies alone, and 2 centers to performing any necrosectomies, while the final 2 centers performed some of each, but in the lowest volume—only in 7 and 13 cases, respectively.

It is important to note the relatively low NIHSS score despite some significant symptoms as suggested by the GCS in this population. This is likely a reflection of the poor assessment of the cerebellar function, but the real impact on alertness in these strokes. There are specific cerebellar assessment scores that would be important to include in future studies of posterior fossa strokes, such as the Scale for the Assessment and Rating of Ataxia (SARA) or the International Cooperative Ataxia Rating Scale and its modifications (MICARS)(Choi et al, 2018; Nickel et al, 2018; Schmahmann et al, 2009). Collaborative research between more institutions, even in a retrospective fashion, may allow better investigation of the impact of time-to-surgery, necrosectomy, and brainstem involvement in the outcome of surgery for large cerebellar infarctions.

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