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Long-term functional outcome after decompressive suboccipital craniectomy for space-occupying cerebellar infarction

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ABSTRACT

Objectives: Suboccipital decompressive craniectomy (SDC) is considered the best treatment option in patients with space-occupying cerebellar infarction and clinical signs of deterioration. The primary purpose of this study was to evaluate long-term functional outcome in patients one year after SDC for space-occupying cerebellar infarction, and secondly, to determine factors associated with outcome.

Patients and methods: All patients treated with SDC due to space-occupying cerebellar infarction between January 2009 and October 2015 were included in the study. Data was retrospectively collected from patient records, CT/MRI scans and surgical protocols. Long-term functional outcome was determined by the modified Rankin Scale (mRS) and mRS ≥ 4 was defined as unfavorable outcome.

Results: Twenty-two patients (16 male, 6 female) were included in the study. Median age was 53 years. Nine patients were treated with external ventricular drainage as an initial treatment attempt prior to SDC. Median time from symptom onset (stroke ictus) to initiation of the SDC surgery was 48 h (IQR 28–99 hours) and median GCS before SDC was 8 (IQR 5–10). At follow up, median mRS was 3 (IQR 2–6). Outcome was favorable (mRS 0–3) in 12 patients and unfavorable in 10 (3 with major disability, 7 dead). Brainstem infarction and bilateral cerebellar infarction were associated with unfavorable outcome.

Conclusions: In this small study, functional long-term outcome in patients with space-occupying cerebellar infarction treated by SDC was acceptable and comparable to previously published results (favorable outcome in 54% of patients). Brainstem infarction and bilateral cerebellar infarction were associated with unfavorable outcome.

1. Introduction

Patients with cerebellar infarction often present with symptoms of nausea, dizziness, vomiting, headache, ataxia or oculomotor dysfunction [1,2]. Development of cerebellar edema in the restricted posterior fossa is a critical complication, which occurs in 17–54% of the patients [3]. The maximum swelling is often reached two to four days after stroke ictus and can cause life-threatening complications such as brainstem compression, obstructive hydrocephalus and transforaminal or transtentorial herniation [1,3–6]. Due to unspecific symptoms and low sensitivity of CT imaging in diagnosing mass effect in the posterior fossa, developing edema is often not recognized before the patient clinically deteriorates [7]. The mortality rate in untreated patients with decreased level of consciousness and signs of brainstem compression due to ischemic cerebellar edema, has previously been estimated at about 80% [8].

A prospective randomized clinical trial (RCT) would be the optimal study design to investigate the appropriate intervention for patients with space-occupying cerebellar infarction. However, the high mortality rate in patients not treated with suboccipital decompressive craniectomy (SDC) makes randomization against conservative treatment ethically problematic, and therefore a future RCT in this area is unlikely. Despite the lack of RCTs, The American Stroke Association and The European Stroke Organization recommend SDC in patients with clinical deterioration due to space-occupying cerebellar infarction [9,10]. A number of reports, primarily retrospective studies, have

Abbreviations: AICA, anterior inferior cerebellar artery; BAEP, brainstem auditory evoked potential; CSF, cerebrospinal fluid; DHC, decompressive hemicraniectomy; EVD, external ventricular drain; SDC, suboccipital decompressive craniectomy; GCS, glasgow coma scale; ICP, intracranial pressure; IRQ, interquartile range; MCA, middle cerebral artery; mRS, modified Rankin Scale; PICA, posterior inferior cerebellar artery; RCT, randomized clinical trial; SCA, superior cerebellar artery; SEP, somatosensory evoked potential

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stated that decompression of the posterior fossa reduces mortality, but only a few studies report data on long-term functional outcome in survivors [1,11–14]. In these patient cohorts with study populations ranging from 10 to 56 patients, favorable outcome (defined as mRS ≤2 or ≤3) is reported in 52–77% of patients and only concomitant brainstem infarction is consistently reported to be a risk factor for unfavorable outcome [1,2,7,13].

The lack of evidence from RCTs makes it even more important to share information from patient cohorts for the benefit of future patients including current surgical practice; patient selection and long-term outcome. Accordingly, the aim of this study was to evaluate the functional independence of patients (favorable outcome) one year after suboccipital decompressive craniectomy (SDC) for space-occupying cerebellar infarction, and to identify factors associated with unfavorable outcome.

2. Patients and methods

2.1. Study population

All patients treated with SDC for a cerebellar infarction at Rigshospitalet (Copenhagen, Demark) between January 2009 and October 2015 were included in this retrospective study. Surgical indication was made by the neurosurgeon specialist on call and follows the concept outlined in the paper by Neugebauer et al., with the exception of neurophysiological assessment of brainstem reflexes [7]. In short, patients with CT/MRI verified cerebellar infarction with edema, decreasing level of consciousness to Glasgow Coma Score (GCS) < 13, previous functional independence and no co-mortibities contra-indicating a neurosurgical procedure of this magnitude are considered for surgery. Patients were excluded from the study, if follow-up data one year after surgery was not available.

2.2. Patient characteristics

Twenty-three patients with cerebellar infarction treated with SDC were identified. One patient was excluded due to missing follow-up data, leaving 22 patients for analysis. Sixteen of 22 patients were male and the median age was 53 years (IQR 32–72 years, see Table 1). The majority of patients (15/22) had at least one documented cardiovascular risk factor such as smoking (10/18), diabetes mellitus (1/22), hypertension (4/22), atrial fibrillation (2/22), ischemic heart disease (1/22) or hypercholesterolemia (3/22).

Information about necrosectomy, resection of the C1-arch and preoperative GCS was unfortunately not available for one patient, leaving 21 patients for further analysis of these factors.

2.3. Surgical procedure

The SDC was performed in accordance with department guidelines and previously published descriptions of the surgical technique [7]. Resection of the C1-arch, duraplasty or infarct evacuation was optional. An external ventricular drain (EVD) was placed in the right lateral ventricle to monitor intracranial pressure (ICP) and, if needed, drain cerebrospinal fluid (CSF). The EVD was either inserted before the decompressive surgery in an attempt to prevent need of a SDC by decreasing the pressure, or in conjunction with the SDC. Timing of the SDC depended on the clinical course and the decision to operate was made based on clinical signs of deterioration and documentation of space-occupying cerebellar infarction on a CT/MRI scan.

2.4. Data acquisition

Comprehensive electronic medical records and radiological investigations from all patients were analyzed. Collection and storage of patient data was approved by the Danish Patients Safety Authority (3-3013-2221/1) and by the Danish Data Protection Agency (RH-2012-58-0004).

Table 1
Baseline data.

Patients characteristics		
Age (median, (IQR))		53 (45-62)
Gender (male)		16/22 (73%)
Vascular risk factors		
Atrial fibrillation		2/22 (9%)
Ischemic heart disease		1/22 (5%)
Diabetes mellitus		1/22 (5%)
Hypertension		4/22 (18%)
Hypercholesterolemia		3/22 (14%)
Smoking		10/18 (56%)
Level of consciousness		
Preoperative GCS ≤ 8		12/21 (57%)
Preoperative GCS (median, (IQR))		8 (5-10)
Postoperative GCS (median, (IQR))		14 (10-15)
Infarct location		
	PICA	19/22 (86%)
	SCA	10/22 (46%)
	AICA	8/22 (36%)
	Unilateral	16/22 (73%)
	Bilateral	6/22 (27%)
	Brainstem	4/22 (18%)
Infarct etiology		
Dissection of the vertebral artery		8/22 (36%)
Basilar artery occlusion		3/22 (14%)
Vertebral artery occlusion		1/22 (5%)
Unknown		10/22 (45%)
Time factors		
Hours between ictus and surgery (median, (IQR))		48 (28-99)

PICA = posterior inferior cerebellar artery.
SCA = superior cerebellar artery.
AICA = anterior inferior cerebellar artery.

All infarctions were documented by a CT scan (and in some cases by a MRI) from which the location of the infarction was identified. Arterial dissection or embolic occlusion as the cause of the cerebellar infarction was determined by CT angiography.

Long-term functional outcome was determined using the modified Rankin Scale (mRS) one year after the SDC (Table 2). If mRS was not directly reported in the electronic medical record, two medical doctors independently evaluated the mRS retrospectively from clinical descriptions in patient records including entries from doctors, nurses and physiotherapists. Disunity in scores lead to discussions about the specific patient in order to obtain a joint decision.

2.5. Statistical methods

Unfavorable outcome was defined as mRS ≥ 4 [15–17]. Prespecified prognostic factors investigated for an association with unfavorable outcome were: age ≥ 60, GCS ≤ 8 before surgery, brainstem infarction, bilateral infarction and time between symptom onset (stroke ictus) and surgery. Furthermore, we analyzed the association between different surgical treatments (EVD before SDC, resection of C1-arch and infarct evacuation) and outcome.

Continuous data are reported as medians with interquartile range (IRQ). Univariate regression analysis with Fisher's exact test was used to determine possible prognostic factors for categorical data and Mann-Whitney *U* test (Wilcoxon Rank Sum) for continuous data. Patient survival is illustrated using a Kaplan-Meier plot. A p value < 0.05 was considered significant in all statistical analyses. All analyses were performed using SPSS Statistics 24.

3. Results

3.1. Clinical status, radiological findings and surgical management

Preoperatively, median GCS was 8 (IQR 5–10) and 12 patients had a

Table 2
Modified Rankin Scale (mRS).

0	No symptoms at all
1	No significant disability despite symptoms; able to carry out all usual duties and activities
2	Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance
3	Moderate disability; requiring some help, but able to walk without assistance
4	Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance
5	Severe disability; bedridden, incontinent and requiring constant nursing care and attention
6	Dead

GCS ≤ 8 (Table 1). In the 17 patients who survived the initial period, median postoperative GCS was 14 seven days after the SDC (IQR 10–15). Median time from symptom onset to surgery was 48 h (IQR 28–99 hours).

Etiologies of the cerebellar infarction were vertebral artery dissection (8/22), basilar artery occlusion (3/22) and vertebral artery occlusion (1/22). Ten patients had an unknown infarct etiology. CT/MRI scans revealed that 16 patients had unilateral infarction and 6 patients had bilateral infarction. The posterior inferior cerebellar artery (PICA) was the most commonly affected artery (19/22), followed by the superior cerebellar artery (SCA, 10/22) and the anterior inferior cerebellar artery (AICA, 8/22). In the 6 patients with bilateral infarctions, SCA and AICA were found to be the most frequently affected arteries. In this subgroup, two patients had a bilateral SCA occlusion and two patients had a bilateral AICA or PICA infarction. A combination of bilateral infarction of AICA + SCA and PICA + AICA + SCA was seen in 1 patient respectively.

All 22 patients were treated with external ventricular drainage and 9 received the EVD before the decision to perform SDC was made (Table 3). Infarct evacuation was performed in 14 patients and resection of the C1 arch in two patients.

3.2. Long-term outcome

At one-year follow-up, 12/22 patients had favorable functional outcome (mRS 0–3) and 10/22 had unfavorable outcome (mRS 4–6). Seven of the 22 patients were dead and 3/10 patients lived with major disability (mRS 4–5). Median mRS was 3 (IQR 2–6). Distribution of the mRS scores is presented in Fig. 1.

Five of 7 patients who did not survive, died within a week after SDC. The remaining two patients died after two and six months respectively (Fig. 2).

Table 3
Factors associated with unfavorable outcome (mRS ≥ 4).

	mRS ≤ 3	*mRS ≥ 4*	*p*
Patient factors			
Age ≥ 60 (*n*)	3/12 (25%)	4/10 (40%)	0.65
GCS ≤ 8 (*n*)	6/12 (50%)	6/9 (67%)	0.66
Bilateral infarction (*n*)	0/12 (0%)	6/10 (60%)	0.03 *
Brainstem infarction (*n*)	0/12 (0%)	4/10 (40%)	0.03 *
Treatment factors			
EVD as initial treatment attempt before SDC	6/12 (50%)	3/10 (30%)	0.42
Infarct evacuation (necrosectomy)	10/12 (83%)	4/9 (44%)	0.16
Resection of the arch of C1	0/12 (0%)	2/9 (22%)	0.17
Hours between ictus and operation, (median, (IQR))	48.0 (33-94)	49.5(19-104)	0.62

GCS = Glasgow Coma Scale, SDC = suboccipital decompressive craniectomy, EVD = external ventricular drain.

* Statistically significant at the level of p ≤ 0.05. Univariate analysis, with Fisher's exact test was used for categorical variables and Mann Whitney *U* test (Wilcoxon Rank sum) for continuous variables.

3.3. Clinical and radiological factors associated with outcome

None of the 12 patients in the group with favorable outcome had brainstem infarction or bilateral infarctions compared to the group with unfavourable outcome, where 4/10 had brainstem infarction ($p = 0.03$) and 6/10 had bilateral infarctions ($p = 0.03$; Table 3).

Among patients with favorable outcome, 3/12 were younger than 60 years of age, compared to 4/10 among those with unfavorable outcome ($p = 0.65$). Six of 12 patients had a preoperative GCS ≤ 8 in the group with favorable outcome compared to 6/9 patients in the group with unfavorable outcome ($p = 0.66$).

None of the registered surgical factors (EVD before SDC, infarct evacuation, C1 arch resection and median time from symptom onset to surgery) were correlated to outcome.

4. Discussion

Patients with space-occupying cerebellar infarction are currently treated with SDC based on clinical experience and data from retrospective studies. In light of the high mortality in patients not treated with SDC [8], future RCTs comparing SDC to conservative treatment are unlikely. Thus, observational studies constitute the current possible option for gathering data to improve definition of predictive indicators. The present study confirms that SDC in patients with space-occupying cerebellar infarction is a lifesaving treatment and identifies occurrence of bilateral infarction or brainstem infarction to be associated with unfavorable outcome at 12 months.

4.1. Long-term outcome

In this report, mortality at follow-up after one year was 32% and a total of 46% had an unfavorable outcome (mRS ≥ 4). There are only few previously published studies examining long-term outcome and they all have a similar retrospective study design and definitions of favorable and unfavorable outcome. In a study by Pfefferkorn et al. (mean follow-up time 5 years), unfavorable outcome was seen in 48% of patients (if unfavorable outcome is defined as in the present study) [1]. In a study by Jüttler et al., unfavorable outcome was seen in 49% of patients (median follow-up time 8 years) [11]. And finally, in a study by Tsitsopoulos et al. investigating SDC in patients with both unilateral and bilateral cerebellar infarction, 47% with unilateral infarction and 40% of patients with bilateral infarction, had an unfavorable outcome (in both studies defined as mRS ≥ 3) at a median follow-up time of 67 months (unilateral infarction) and 58 months (bilateral infarction) [2,13]. In a recent systematic review and meta-analysis including 11 studies (including the ones mentioned above) and 283 patients in total, mortality was 20% and 48% of patients had an mRS between 3–6 (unfavorable outcome) at a median follow-up time of 9 years [18].

Surgical decompression is also applied in patients with supratentorial space-occupying cerebral edema, primarily following middle cerebral artery (MCA) infarction known as malignant MCA infarction. In these patients, decompressive hemicraniectomy, (DHC) was compared to best medical treatment in three RCTs including patients ≤ 60 years of age (DECIMAL, DESTINY and HAMLET) [19–21] and in one RCT including patients > 60 years of age (DESTINY II) [22]. The general notion is that patients treated with SDC for space-occupying

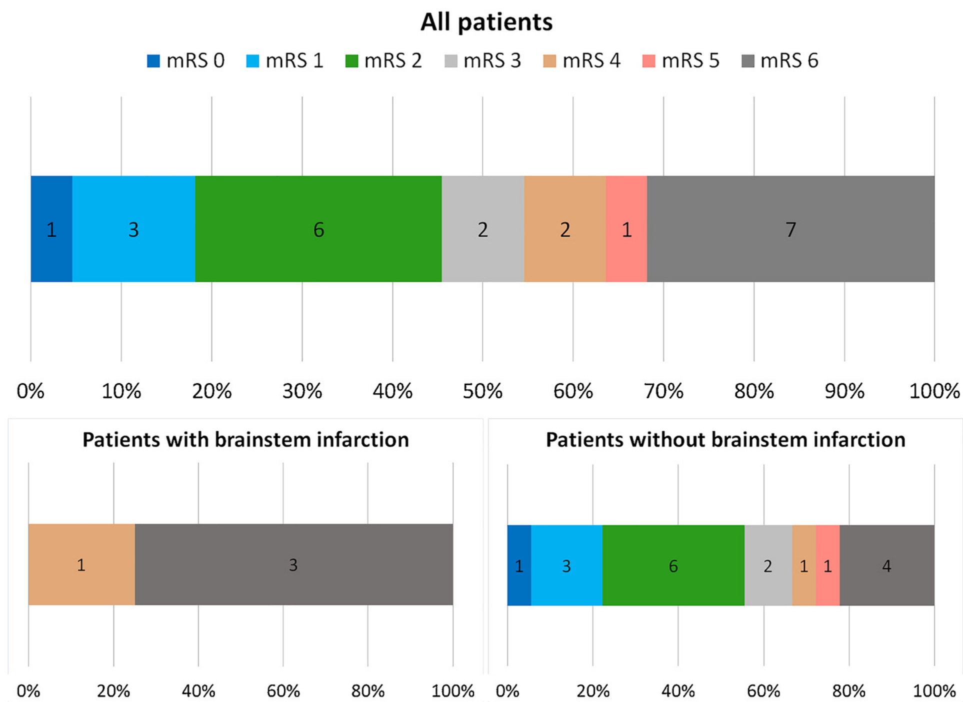

Fig. 1. Distribution of Modified Ranking Scores (mRS) in all patients treated with suboccipital decompressive craniectomy for space-occupying cerebellar infarction and in the same patients divided according to radiological evidence of concomitant brainstem infarction.

cerebellar infarction have better outcome than patients treated with DHC for malignant MCA infarction, due to lesions with larger volumes and more functional damage in supratentorial infarctions. In a combined analysis of DECIMAL, DESTINY and HAMLET, the authors report a mortality of 22% in the surgically treated group and a prevalence of unfavorable outcome (defined at mRS 5–6) of 26% at 12 months [23]. If unfavorable outcome is defined as in the present study (mRS ≥ 4), the figure is 57%. Thus, the data in the present study and in previous retrospective studies support the notion that outcome is better in patients treated with SDC for space-occupying cerebellar infarction compared to

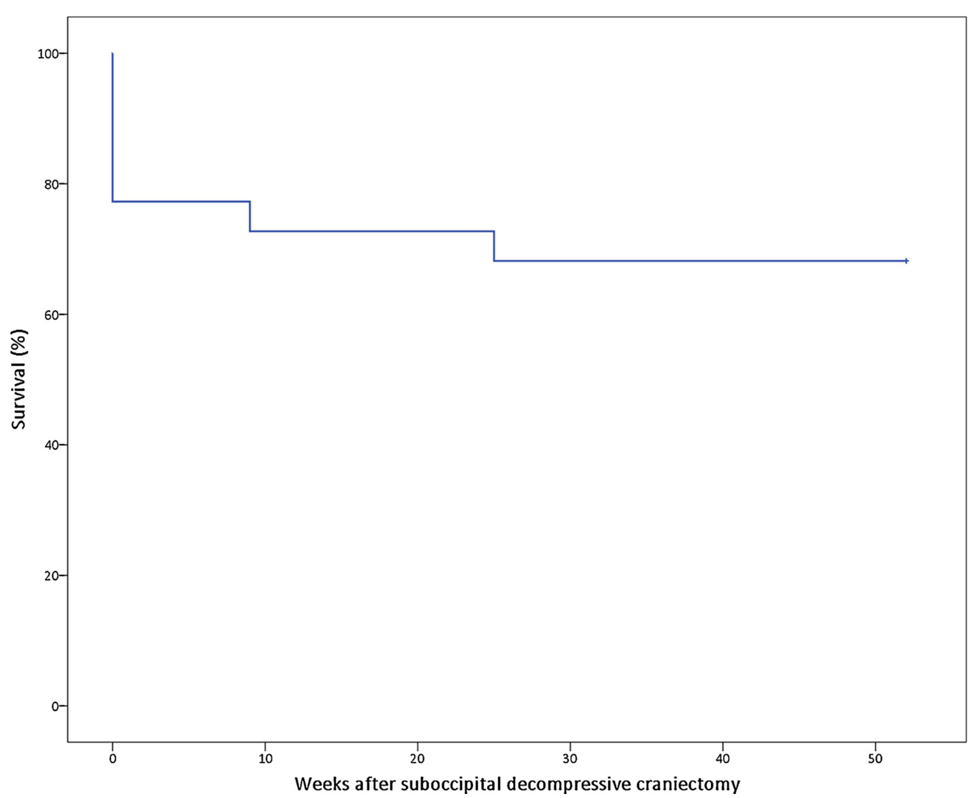

Fig. 2. Kaplan-Meier curve of patient survival after suboccipital decompressive craniectomy (SDC) for space-occupying cerebellar infarction. Five patients died within a week after SDC. The remaining two died after two and six month respectively.

patients treated with DHC for malignant MCA infarction, although the difference is not substantial.

4.2. Vascular territories and extent of infarction

The PICA has previously been found to be the most commonly affected artery [1,24]. This corresponds well with our results where involvement of the PICA territory was found in 19/22 patients. In 10 of these patients, infarction was limited to this vascular territory. The SCA was found to be the second most affected artery (10/22) and AICA the least frequently involved (8/22). Infarction in the AICA territory led to surgery only in conjunction with infarctions in other vascular territories [1,24]. This means, that clinicians should pay particular attention to patients with PICA territory infarctions, although other infarctions (especially when combined) can lead to cerebellar edema requiring SDC.

Previous studies have discussed the influence of bilateral infarction on functional outcome. Bilateral infarctions are rare and data regarding these patients is very scarce [25]. Pfefferkorn et al. concluded that outcome was similar in patients with unilateral and bilateral infarction [1]. In another study, which included 162 patients with acute cerebellar infarction, bilateral infarction was an independent predictor of unfavorable outcome (mRS $\geq$ 3) at discharge [24]. In our patient cohort, we found a significant association between bilateral cerebellar infarction and unfavorable outcome.

The benefit of SDC in patients with radiological evidence of brainstem infarction is widely discussed. In the present series, brainstem infarction was associated with unfavorable outcome in agreement with previous studies [1–3]. We recommend a fast MRI protocol with FLAIR and DWI sequences preoperatively, if the patient's condition allows surgical delay by further imaging. Neugebauer et al. recommended the use of brainstem auditory evoked potential (BAEP) and somatosensory evoked potential (SEP) to determine the best suited treatment for comatose patients [7]. This diagnostic approach is not routinely performed in our clinic.

Bilateral infarction and brainstem involvement could not be established as independent predictors of unfavorable outcome due to our small study population. For the same reason, the analyses of other prognostic factors should be interpreted with caution.

4.3. Other possible outcome predictors

Some previous studies have identified level of consciousness before SDC as a strong predictor of long-term outcome [3,5,11,13,18,26,27]. In another study, this association was not found, supporting an active surgical strategy also in cases presenting with a low GCS [1]. Conflicting results are also found considering the impact of age on functional outcome [1,3,11,13,18,26]. The results from the present study support the view that deterioration to a comatose state (GCS $\leq$ 8) should not in itself contradict a decision of surgical intervention. However, it is reasonable to believe that the time from deterioration to surgery might influence functional outcome, and patients with cerebellar infarctions should be observed in or close to a neurosurgical department to minimize this time. Furthermore, at least in our relatively young patient population, age above 60 does not seem to have a negative impact on long-term functional outcome.

Resection of infarcted tissue is thought to increase the effect of the SDC by reducing mass-effect and the following cytotoxic response [1]. In a systematic review and meta-analysis by Ayling et al., resection of infarcted tissue was reported to be associated with favorable outcome [18]. Other studies did not find this association, which is in accordance with our series [1,11].

In our study, the median time between symptom onset (stroke ictus) and surgery was 48 h (IQR 28–99). We found no association between time from ictus to surgery and functional outcome. Furthermore, outcome was not statistically affected by EVD insertion as an initial treatment attempt before SDC, or in conjunction with the decompressive surgery. Our study therefore supports the current clinical practice of surgical intervention in cases with clinical deterioration.

5. Limitations

Our study design is retrospective and the number of patients is relatively small, preventing us from drawing clear conclusions regarding independent factors related to favorable/unfavorable outcome. Furthermore, most patients underwent a CT scan and not an MRI scan, which would have been the optimal modality for visualizing ischemic lesions in the posterior fossa and brainstem. The long-term functional outcome assessment was in some cases retrospectively derived from patient records. This has previously been found to be a less valid way of scoring mRS compared to face-to-face or telephone interviews [28]. In our patient records, clinical information from both doctors, nurses and physiotherapists are available and we believe that this information allowed us to assess mRS with sufficient confidence to dichotomize the outcome in favorable/unfavorable.

6. Conclusion

SDC is a lifesaving procedure in patients with clinical deterioration due to space-occupying cerebellar infarction. In our study population, long-term functional outcome was found to be in line with previously published studies, i.e. favorable (mRS 0–3) in about half of the patients. Risk factors for unfavorable outcome were bilateral cerebellar infarction and concomitant brainstem infarction, which implicates that a conservative strategy should be considered in patients presenting with these extensive strokes. To be able to identify patients that benefit from surgery for space-occupying cerebellar infarction in the future, we encourage clinicians to publish their case series, including individual patient data, allowing meta-analytical combination of data for larger investigations of independent risk-factors for unfavorable outcome.

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Declarations of interest

None.

Ethical approval

This article does not contain any studies with human participants performed by any of the authors. For this type of study formal consent is not required.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.clineuro.2018.11.023.

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