

Decompressive Craniectomy in Patients with Aneurysmal Subarachnoid Hemorrhage: A Single-Center Matched-Pair Analysis

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Key Words

Decompressive craniectomy · Aneurysmal subarachnoid hemorrhage · Outcome

Abstract

Background: The role of decompressive craniectomy (DC) in aneurysmal subarachnoid hemorrhage (aSAH) patients is still controversial. In this study we evaluated the effect of DC for aSAH patients. **Methods:** A matched-pair analysis was performed to compare the outcomes of patients with DC to those of patients without DC. Among 295 consecutive aSAH patients, 56 required DC. Of the remaining group, 56 matched controls were found. The match was conducted on the basis of epidemiological and potential prognostic factors, such as age, gender, World Federation of Neurosurgical Societies (WFNS) grade, Fisher group and occurrence of vasospasm. **Results:** Fifty-four of 56 (96.4%) patients with DC were dependent or dead at 1 month, compared with 49 of 56 (87.5%) without DC. There was no significant difference between the groups ($p = 0.16$). One-year outcomes were available for 108 patients (96.4%). Thirty-nine of 54 (72.2%) patients treated with DC were dependent or dead at 1 year, compared with 30 of 54 (55.6%) patients in the control group. There was no significant difference between the groups ($p = 0.11$). This re-

sult was unaffected by age, sex and WFNS grade. Subgroup analyses whether DC was performed primarily or delayed, and whether DC was performed due to spasm, hematoma or vessel occlusion failed to detect any significant difference. **Conclusion:** There was no significant advantage for patients treated with DC, but more than 25% achieved a good long-term outcome. While the value of DC is deemed uncertain, it may be effective for a very specific subset of aSAH patients. Further comparative studies are needed to resolve this matter.

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Introduction

Decompressive craniectomy (DC) has been shown to improve outcome in patients with massive ischemic infarction and severe head injury [1–4]. However, the role of DC in aneurysmal subarachnoid hemorrhage (aSAH) patients is still controversial [5–11]. In aSAH patients, brain swelling can occur primarily (due to initial brain damage and/or intracranial hemorrhage) and secondarily (due to vaso-

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spasm and/or infarction). Due to the heterogeneity of these reasons, the true value of DC in aSAH patients remains controversial. We hypothesized that DC could improve the outcome in patients with aSAH similar to DC for massive ischemic infarction and severe head injury. The aim of this study was to reveal the value of DC in aSAH patients.

We analyzed the outcome of aSAH patients who were treated with DC. A matched-pair analysis was performed to compare outcomes of patients with DC to a second cohort of aSAH patients who were treated without DC. The match was conducted on the basis of epidemiological and potential prognostic factors, such as age, gender, World Federation of Neurosurgical Societies (WFNS) grade [12, 13], Fisher group [14] and occurrence of vasospasm [15–17].

We compared the 1-month and 1-year outcomes in these two groups retrospectively and evaluated the effect of DC for aSAH patients.

Subjects and Methods

From January 2004 to July 2009, 295 aSAH patients were treated with clipping or coiling at a single university hospital (corresponding author's institution). All aSAH patients' data were prospectively entered into a database, which were available for the retrospective analysis. Among them, 56 required DC as judged by the treating neurosurgeon. Of the remaining group, 56 matched controls were found for matched-pair analysis. The match was conducted on the basis of epidemiological and potential prognostic factors, such as age, gender, WFNS grade [12, 13], Fisher group [14] and occurrence of vasospasm [15–17].

Outcome was assessed by the extended Glasgow Outcome Scale (eGOS) [18, 19] and checked by telephone interview and/or during follow-up in our outpatient clinic.

Ethics approval for the study protocol including secondary approach of the given patient population for outcome assessment was granted by the local ethics committee.

Clinical Management

All aSAH patients were admitted to the neurosurgical or neurological intensive care unit. A policy of early aneurysm treatment was followed in all patients. Patients underwent either surgical clipping or endovascular coiling for treatment of the ruptured aneurysm within 72 h. Posterior circulation aneurysms were mostly treated interventionally, whereas anterior circulation aneurysms were more likely to be treated surgically. Patients with bilateral pupillary dilatation received treatment, when pupils were not fixed yet or responded to mannitol administration. An intraparenchymatous intracranial pressure (ICP) sensor (Codman microsensor, Johnson and Johnson, Raynham, Mass., USA) or ventricular drainage catheter was inserted before or after the definitive treatment.

After surgery the patients were maintained in a normotensive, normovolemic, normoglycemic and normothermic state as much as possible. Oral nimodipine was administered during the first 3

weeks after aSAH (6×60 mg/day). Treatment of vasospasm was initiated as necessary with hypertensive, hypervolemic and hemodilutional therapy, as diagnosed by the clinical appreciation of neurostatus deterioration in combination with parameters of invasive monitoring (i.e. regional cerebral blood flow, microdialysis), angiographic studies (if needed) and/or transcranial Doppler studies (defined by flow velocities >200 cm/s) and with the exclusion of other possible causes such as hydrocephalus, hemorrhage, sepsis, etc. Glasgow Coma Scale and pupil examinations were carried out hourly. Treatment of increased ICP was initiated, when necessary, using ventricular cerebrospinal fluid drainage, osmotherapy (mannitol, hypertonic saline) and/or increased sedation (incl. barbiturate coma with thiopental, titrated to an electroencephalographic burst suppression pattern). Any sustained, therapy-refractory increase in ICP >20 – 25 prompted a clinical case discussion for decompressive hemicraniectomy.

Decompressive hemicraniectomy was performed in a standardized fashion by elevation of a bone flap of at least 12 cm in diameter (including the frontal, parietal, temporal and the occipital squama). Additional temporal bone was removed so that the floor of the middle cerebral fossa was decompressed. Bone flaps were kept under sterile conditions and cryoconserved at -80°C . In survivors reimplantation was performed between 3 and 6 months after hemorrhage.

Clinical Signs of Herniation and ICP Changes

All patients' charts and other documentation were thoroughly checked for clinical signs of herniation and ICP changes to compare the severity of injury in both groups of mainly high-grade aSAH patients. Clinical signs of herniation (i.e. anisocoria and bilateral pupil dilatation) were checked between the day of onset and SAH day 14. Furthermore, in the DC group, every patient's maximum ICP before DC, just after DC and maximum ICP after DC within the first 14 days after SAH were checked. In the control group, maximum ICP values within the same time span were checked. We recorded only values which continued for at least 1 h.

Statistical Methods

The distribution of baseline patient characteristics was compared between groups using descriptive statistics. The χ^2 and Fisher's exact tests for paired data were used to test for differences in distributions between groups. The Mann-Whitney U test was used to compare nonparametric data. A p value of <0.05 was considered statistically significant.

All analyses were performed using a commercially available statistical software package (Prism4.0; GraphPad Software, La Jolla, Calif., USA).

Results

Comparability of Patients

In table 1 the distributions of patient characteristics between the DC group and control group are listed. A total of 112 aSAH patients (50.5 ± 11.8 years old, range 27–79, median WFNS score: 5) were enrolled. Control patients were matched successfully with the exception of

Table 1. Characteristics of the patient cohort who underwent DC and the control group ('matched pairs')

Patients	DC total	Control	p value
Male:female ratio	22:34	22:34	1
Age, years	50.1 (27–77)	51.5 (27–79)	0.51
WFNS SAH score			
1	6	7	
2	3	2	
3	1	2	0.94
4	13	11	
5	33	34	
Median WFNS score	5	5	
Fisher grade			
3	28	31	
4	28	25	0.71
Location			
Anterior circulation	55	49	
Posterior circulation	1	7	0.06
Treatment			
Clip	49	36	
Coil	7	20	0.007
Spasm			
Yes	43	41	
No	13	15	0.83

Age, gender, WFNS score, Fisher grade, aneurysm location and occurrence of cerebral vasospasm were successfully matched. There were more patients in the DC group who also underwent aneurysm obliteration by clipping, especially when located on segments of the middle cerebral artery.

aneurysm location. There were more patients in the DC group who also underwent aneurysm obliteration by clipping, especially when located on segments of the middle cerebral artery. Seven patients in the DC group and 19 patients in the control group were treated by coiling.

Clinical Outcome

Outcome measures were assessed at 1 month and 1 year after treatment. Figure 1a shows the outcome of 112 patients at 1 month. Fifty-four of 56 (96.4%) patients treated with DC were dependent or dead (eGOS 1–4) at 1 month, compared with 49 of 56 (87.5%) treated without DC. There was no significant difference between the groups ($p = 0.16$).

At 1 year outcome data were available for analysis in 108 out of 112 patients (96.4%). Follow-up was missing for 2 patients treated with DC and 2 patients treated without DC. These had achieved eGOS of 2 and 3 in both groups at the 1-month outcome assessments. Thirty-

Table 2. Characteristics of the patient cohort who underwent DC according to outcome (favorable outcome eGOS 5–8, unfavorable outcome eGOS 1–4)

DC patients	eGOS 5–8	eGOS 1–4	p value
Male:female ratio	5:10	17:22	0.76
Age, years	48.1 (39–64)	50.9 (27–78)	0.21
WFNS SAH score			
1	2	4	
2	1	2	
3	1		0.13
4	4	9	
5	7	24	
Fisher grade			
3	9	19	
4	6	22	0.55
Location			
ACA	4	6	
Posterior circulation	1	0	
ICA	right 1 left 1	3 4	0.02
MCA	right 2 left 6	11 13	
Treatment			
Clip	11	36	
Coil	4	3	0.08

Age, gender, WFNS score, Fisher grade and treatment option (coiling vs. clipping) were compared and found noncontributory. Outcome varied significantly according to aneurysm location (small numbers). ACA = Anterior cerebral artery; ICA = internal carotid artery; MCA = middle cerebral artery.

nine of 54 (72.2%) patients treated with DC were dependent or dead at 1 year, compared with 30 of 54 (55.6%) patients treated without DC. Among 52 dependent patients at 1 month, 13 patients recovered to more than eGOS 5 in the DC group. Among 49 dependent patients at 1 month, 12 patients recovered to more than eGOS 5 in the matched group. There was no significant difference between the groups ($p = 0.1085$; fig. 1b). This result was unaffected by age, sex and WFNS grade. Furthermore, subgroup analyses whether DC was performed primarily or in a delayed fashion, and whether DC was performed due to spasm, hematoma or vessel occlusion failed to detect any significant difference in 1-month and 1-year outcomes. In 25 primary DC patients, no patient suffered from rerupture of the aneurysm during and after the DC before obliterating the aneurysm by clipping or coiling. There was no surgical morbidity and mortality of DC (including procedures for reimplantation of the bone flap) in this study.

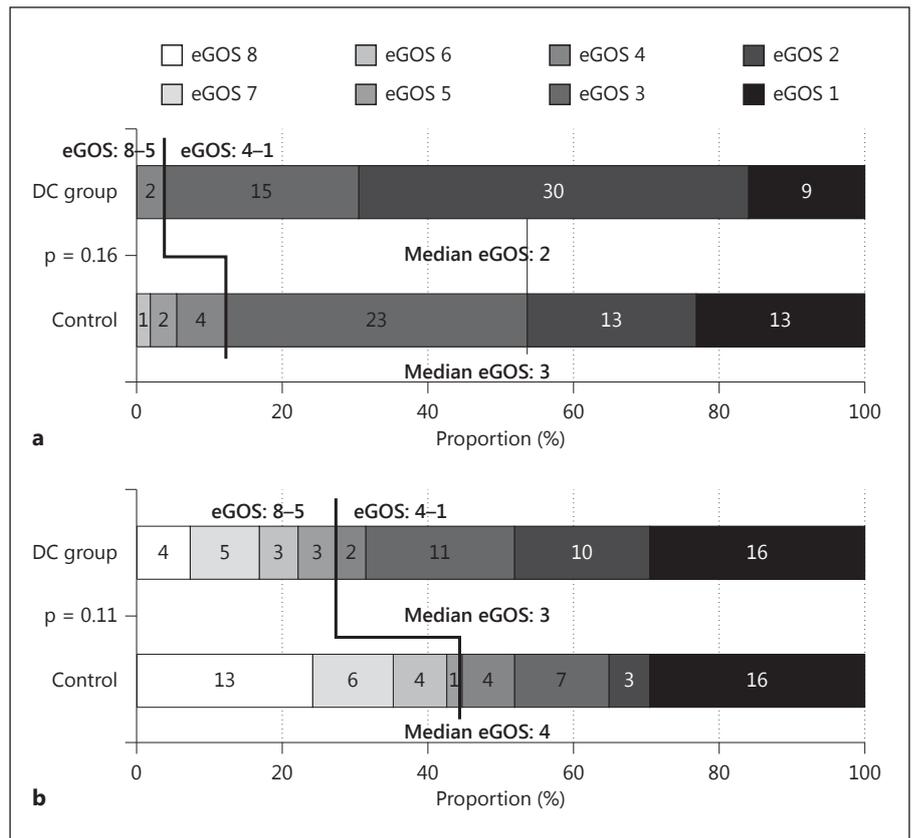


Fig. 1. Outcome according to the eGOS. Outcome of DC patients and control patients 1 month (a) and 1 year following SAH (b). There was no significant difference between the groups.

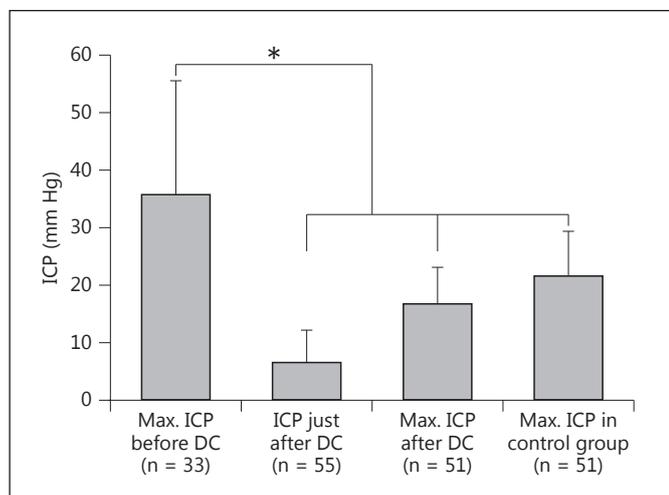


Fig. 2. Comparison of ICP within and between the groups. The maximum ICP before DC was 36.1 ± 19.3 mm Hg (median: 30), and the maximum ICP in the control group was 21.7 ± 7.50 mm Hg (median: 21). There are statistically significant differences between all columns ($p < 0.001$).

Clinical Signs of Herniation and ICP Changes

Anisocoria and bilateral pupil dilatation were present in 24 patients (21: anisocoria, 3: bilateral pupil dilatation) of the DC group and in 3 patients (1: anisocoria, 2: bilateral pupil dilatation) of the control group. There was a significant difference between the groups ($p < 0.0001$). Most poor-grade aSAH patients (including control group patients) had intraparenchymal ICP sensors and ICP was measured hourly. Figure 2 shows the maximum ICP before DC, just after DC and the maximum ICP after DC or within 14 days following SAH in the control group. Three patients in the primary DC group underwent preoperative ICP monitoring. There were significant differences between the groups. Mean maximum ICP before DC, ICP just after DC, maximum ICP after DC and maximum ICP in the control group were calculated as 36.1 ± 19.3 mm Hg (median: 30), 6.67 ± 5.63 mm Hg (median: 5), 16.9 ± 6.17 mm Hg (median: 16) and 21.7 ± 7.50 mm Hg (median: 21). In terms of WFNS grade and Fisher group, the SAH severity of both groups was matched successfully. However, mean and median ICP values were significantly different between the groups.

Discussion

The role of DC in aSAH patients is still controversial [5–10]. Some groups reported retrospectively on their own results without a control group (Smith et al. [10]: 8 patients, Buschmann et al. [5]: 38 patients, Schirmer et al. [9]: 16 patients, Otani et al. [8]: 57 patients, Güresir et al. [7]: 79 patients, Dorfer et al. [11]: 66 patients). The present study was conducted as a matched-pair analysis to assess the effectiveness of DC. Our results are similar to those of D'Ambrosio et al. [6], who reported that DC failed to prolong short-term survival and the overall outcomes in a 22 patient (12 DC patients; 10 control patients) data analysis. In aSAH patients, brain swelling can occur primarily (due to initial brain damage and/or intracranial hemorrhage) and secondarily (due to vasospasm and/or infarction). The complex nature of these pathophysiological cascades and small sample sizes limit direct comparison. Therefore, in this study we analyzed a larger number of aSAH patients who were treated with DC utilizing a matched-pair design which involved similarly injured patients.

We performed 56 DC without relevant surgical morbidity. It has to be underscored that in 25 primary DC patients, none suffered from rerupture before definitive obliteration of the aneurysm by clipping or coiling.

Although we could match the two patient groups successfully, we were unable to avoid selection bias among the groups completely. First of all, the control group did not match with the DC group in terms of the indication for DC (e.g. intractable brain swelling, therapy-refractory intracranial hypertension). Incontrollable elevated ICP might be a highly relevant factor related to the outcome of aSAH patients. Furthermore, there were 24 patients with clinical symptoms of herniation (42.9%) in the DC group, but there were only 3 patients (5.4%) in the control group. However, matching these factors in retrospect is difficult and almost impossible to achieve in a randomized study due to ethical reasons. Under these circumstances most clinicians would not see equipoise to medical treatment, and therefore DC would remain the last resort to control intracranial hypertension. Secondly, baseline characteristics of the two groups were different in a way that treatment of middle cerebral artery aneurysms and surgical clip obliteration was more frequent in the DC group. Although this association of location, favorite treatment and additional need for decompression appears logical, it may still be a source of error. No better match could be achieved within the limits of the given sample population.

According to our analyses DC did not seem to improve the outcome in poor-grade aSAH patients. There was no significant difference in 1-month and 1-year outcome between the groups, but there were an obvious lower morbidity and mortality in the control group.

Hacke et al. [20] showed that with conventional treatment of elevated ICP up to 78% of the patients with complete middle cerebral artery territory infarction die from transtentorial herniation. Conversely Schwab et al. [3] showed that the outcome of patients treated with DC in severe hemispheric infarction surprisingly improved not only the mortality, but also the functional outcome. The mortality was 16% in the early DC group (DC was performed before the onset of transtentorial herniation) and 34.4% in the late DC group (DC was performed just after the onset of transtentorial herniation). However, DC could not improve the outcome of aSAH patients with elevated ICP to a similar extent as shown in patients with hemispheric infarction. In aSAH patients, initial brain damage, intracranial hemorrhage, vasospasm and infarction interact with each other to increase ICP, and this may lead to a negative spiral resulting in more secondary ischemic brain injury. Increased ICP in aSAH patients is associated with severely deranged cerebral metabolism and poor outcome [21, 22]. In our DC cohort, 24 (42.9%) patients suffered from anisocoria or bilateral pupil dilatation, compared to control patients, with only 3 patients showing clinical signs of tentorial herniation. Maximum ICP before DC was 36.1 ± 19.3 mm Hg (median: 30), and maximum ICP in the control group was 21.7 ± 7.50 mm Hg (median: 21). There were significant differences between the groups. Intracranial hypertension might have affected the outcome, especially in the DC group.

In 24 DC patients with anisocoria or bilateral pupil dilatation, 10 (41.7%) died and 5 (20.8%) achieved a good outcome at 1 year (eGOS: 5–8). Especially in 3 DC patients with bilateral pupil dilation, no patients died. These 3 patients achieved eGOS 8, 3 and 2. In 3 patients of the control group with anisocoria or bilateral pupil dilatation, 1 who suffered from anisocoria on admission recovered to eGOS 7 one year later; however, the 2 patients who suffered from bilateral pupil dilatation during the acute phase after the definitive treatment died from transtentorial herniation. According to the currently published literature, there are 4 studies which individually included more than 20 DC patients. Buschmann et al. [5] reported that a good functional outcome score (Glasgow Outcome Score, GOS, 4 and 5 at 1 year) could be reached in 52.6% (20/38) of the cases. There was no description about patients' clinical signs of transtentorial herniation. In their

series, patients with increasing ICP above 20 mm Hg received DC [5]. Otani et al. [8] reported on 21 patients (36.8%) who recovered to a good outcome (GOS 4 and 5 on discharge) in a series of 57 DC patients. In this paper, the authors focused on Hunt and Kosnik grade IV and V patients with intracerebral or sylvian hematoma. There was no description about patients developing clinical signs of transtentorial herniation. All the patients were treated with DC primarily [8]. Güresir et al. [7] reported that a favorable outcome (modified Rankin Scale 0–3 at 6 months) was attained in 21 (26.6%) of 79 DC patients. Forty-two (53.2%) patients suffered from anisocoria or bilateral pupillary dilatation [7]. Dorfer et al. [11] reported 66 of 964 patients treated for aSAH who underwent DC. Among these 66 DC patients, there were 16 of 46 (34.8%; hematoma group), but only 2 of 20 (10%; edema and ischemia group) who achieved a favorable outcome (modified Rankin Scale 0–3). There was no description about patients' clinical signs of transtentorial herniation [11]. It is easily visible that patients' characteristics and treatment strategy differed significantly between these reports. Moreover, the indication of DC was nonuniform. Outcome figures may therefore not be directly comparable. The third study, however, was obtained at a similar German University Hospital Center with high expertise in cerebrovascular disorders. Interestingly, 6-month outcomes compared quite well with 1-year results from the current study. We failed to show a significant advantage of DC for aSAH patients. On the other hand, more than 25% DC patients achieved a good outcome. Compared with previous reports, this outcome is acceptable. Therefore DC can be effective in a specific subset of aSAH patients. However, the sample size of 56 DC patients in this study may be too small to reveal the true value of DC for aSAH. Furthermore, we did not consider other confounding factors, such as hypertension, diabetes, dyslipidemia, smoking and excess drinking. These confounding factors might have affected the outcome of patients with in this study.

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Conclusions

We failed to show a significant advantage of DC for aSAH patients. Intracranial hypertension as a trigger for DC might have affected the outcome within this group of patients irreversibly. On the other hand, more than 25% of DC patients still achieved a good outcome, underscoring that DC can be effective in a specific subset of aSAH patients. Earlier DC might have prevented uncontrollable high ICP (transtentorial herniation) and/or infarction due to the vasospasm finally resulting in a better clinical outcome. Further studies are needed to resolve this matter.

Acknowledgment

We are grateful for the statistical advice of Dr. Takahiro Nakamura at the National Defense Medical College in Japan.

Disclosure Statement

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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