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ORIGINAL COMMUNICATION

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Prognosis of patients after hemicraniectomy in malignant middle cerebral artery infarction

Abstract *Background and Purpose* There are unsatisfactory therapeutic options for treatment of large infarctions of the middle cerebral artery with secondary development of life threatening brain edema. In most cases, post-ischemic brain edema can not be adequately treated by conservative means. However, several studies have shown that operative procedures such as decompressive hemicraniectomy can decrease mortality. Apart from mortality, the morbidity and quality of life are major features with which to estimate therapeutic benefit. The aim of this study was to acquire follow-up data on quality of life and outcome in patients treated with hemicraniectomy after stroke. *Methods* Eighteen patients were treated with decompressive hemicraniectomy after life threatening middle cerebral artery infarction between July 1997 and April 2000 in our clinic. Six patients (33 %) died within the first six months after the procedure. All twelve surviving patients were seen in a follow-up examination 7 to 26 months after the stroke and tested using the Rankin-Scale, Barthel Index (BI), Aachener Life Quality Inventory (ALQI) and Zung Self-Rating Depression Scale. *Results* Survivors with a mean age of 40.7 ± 16.5 years were significantly younger than non-survivors with a mean age of 64.5 ± 9.2 years ($p = 0.006$). Mean Barthel-Index of surviving patients was 61.1 ± 26.1 points, mean Rankin-Scale 3.3 ± 1.2 points. Two patients were able to return to work. Patients younger than 45 years ($n = 7$) had a significantly better outcome (BI 75.7 ± 20.7) than patients over 45 years ($n = 5$) (BI 42.0 ± 22.7 points, $p = 0.026$). Among five patients with an infarction of the left hemisphere, four had a slight to moderate Broca aphasia and one patient a global aphasia. Quality of life assessment by ALQI showed moderate disability (58.0 ± 22.7 of 107 points) with no significant difference between left- and right-hemispheric infarctions. Using the Zung Self-Rating Depression Scale six patients were ranked as slightly depressive, one patient as moderately depressive and five patients as not depressive. Eleven out of twelve survivors, as well as their relatives, approved of the decision to have the operation. *Conclusions* The study provides evidence that hemicraniectomy as treatment of severe space occupying ischemic brain edema saves lives and results in good quality of life in a high proportion of patients, especially in the young. This conclusion is restricted by the lack of a control group, which was deemed unethical in studying a potentially life saving therapy.

Key words malignant MCA infarction · brain edema · hemicraniectomy · quality of life

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Introduction

Life threatening cerebral infarctions of the middle cerebral artery territory are found in 7 to 15 % of all stroke patients [23, 37]. Embolic or thrombotic occlusion of the internal carotid artery or proximal segments of the middle cerebral artery can lead to territorial infarction and development of large ischemic areas. Patients show severe neurological deficits with hemiplegia, head and

gaze deviation towards the side of infarction and can have deterioration of consciousness. Brain edema subsequently may be associated with transtentorial brain herniation and death [9, 18, 30]. For this kind of life threatening ischemic cerebral infarction the term of "malignant middle cerebral artery infarction" was introduced by Hacke et al. in 1996 [9]. Young patients are affected more often since they do not have atrophic cerebral tissue and enough space to compensate for brain swelling [9, 10, 11, 12]. Mortality is up to 78 % if only conservative treatment of brain edema with hyperventilation, osmotherapy, barbiturate- or THAM buffer infusions are used [1, 10, 34]. Recent studies have shown that early decompressive hemicraniectomy decreases mortality to 16–42 % [4, 6, 15, 16, 17, 26, 27, 31, 32, 33, 34, 38]. The aim of decompressive surgery is to give room for expansion of the swelling, restore cerebral perfusion and optimize retrograde perfusion through leptomeningeal collateral vessels [7, 40]. Since young patients are especially affected by malignant middle cerebral infarctions, in addition to reducing the death rate, lowering morbidity and improving quality of life are essential goals of decompressive hemicraniectomy. The aim of this study was to assess data of long term outcome and the measures that represent quality of life after decompressive hemicraniectomy in malignant MCA infarction.

Subjects and methods

Decision for hemicraniectomy was made in eighteen consecutive patients with clinical signs of severe middle cerebral artery syndrome not showing other underlying serious medical diseases between July 1997 and April 2000. Patient data and surgery data at inclusion were collected retrospectively. The patients had the following computed tomography (CT) criteria: loss of the corticomedullary contrast or hypodense area of more than 50 % of the middle cerebral artery territory, disappearance of gyri, compression of the lateral ventricles, ipsilateral enlargement of the ambient cistern and/or compression of the basal cisterns. Patients either had signs of an excessive rise of intracranial pressure on admission (not manageable by conservative therapy) or all options of conservative therapy had failed. One patient was 76-years-old and underwent decompressive hemicraniectomy after systemic thrombolysis and secondary intracerebral bleeding. The patients' families and – if possible – the patients themselves were informed about the possibilities of conservative and operative therapy, including risk and character of complications as well as the expected mortality and morbidity of the procedure. Since all other treatment options had been exhausted, the operation was classified as a "curing attempt" and agreement was signed by a family member of each patient. A control group with conservative therapy analysis was not used owing to ethical concern of possibly depriving patients of hemicraniectomy as a potentially life-saving therapy.

Conservative treatment

On admission, all patients received oxygen supply via nasal probe (n = 14) or mechanical ventilation (n = 4). Normoglycemia (100–120 mg% glucose), normothermia (≤ 37.5 °C) and high perfusion pressure (MABP ≥ 120mmHg) was obtained by medical treatment and regular checks.

In cardioembolic stroke or after dissection of the carotid artery heparin was used to increase partial thromboplastin time (pTT) up to 2–2.5 times the normal values (n = 13). Three patients received systemic rtPA thrombolysis during the first three hours after stroke (17 %). To reduce elevated intracranial pressure mannitol 10 % and furosemide were given as well as an elevation of 30°of the trunk in all patients.

Operative treatment

Patients were either treated operatively in the Department of Neurosurgery of University Hospital Klinikum Grosshadern (n = 7), the department of Neurosurgery of Krankenhaus-Bogenhausen (n = 1) or by neurosurgically trained surgeons of the Department of Traumatology in Krankenhaus München-Harlaching (n = 10).

The operation procedure was similar in all hospitals and in all patients following the technique of dural augmentation of Delashaw [6]. After skin incision the skull was opened in a paramedian line from occipital to low temporobasal region in a curved line towards the ear, followed by a double T shaped incision of the dura. Mean size of hemicraniectomy was 13.8 ± 2.9cm in the frontotemporal line and 9.3 ± 2.3cm in the temporoparietal line. After the operation the closure was performed with either an introduction of Goretex tissue or autologous galeal augmentation underneath the open dura with selective fixing. Two patients had to undergo operative revision because of progressive brain edema and a partial resection of infarcted temporal areas was performed. Invasive ICP monitoring was done preoperatively in one (6 %) and postoperatively in nine patients (50 %). Reimplantation of the skull was done 2–6 months after the first procedure; two patients received Palacos reconstruction.

Diagnostic procedures

All patients had extra- and transcranial Doppler and Duplex sonography including patent foramen ovale monitoring, transthoracic or transesophageal echocardiography. Two patients had diagnostic conventional angiography. CT was performed on all patients on admission (Somatom DR or Somatron 4 Plus, Siemens without contrast agent with 4 and 8mm thick slices for the brainstem and hemisphere, respectively). Repeat CT was performed if there was clinical deterioration as well as 24 hours after thrombolysis. Most patients had several CT and MRI checks.

Data collection

Personal data, circumstances of the event, etiology and development of the stroke as well as diagnostic and therapeutic data were collected retrospectively from patient and medical records. Clinical findings were documented by NIHSS (National Institutes of Health Stroke Scale), Rankin-Scale and Barthel-Index. A prospective follow-up evaluation of the outcome was performed after a minimum of 7 months (range 7–26 months). Six patients had died in the meantime, but all twelve surviving patients were contacted and examined in person with the following tests [20]: Physical-functional state by National Institute of Health Stroke Scale (NIHSS) [3], activities of daily living by Barthel-Index [8, 19], participation of socio-cultural life by the Rankin-Scale [24] and the ability to participate in work. Psychological status was judged by Zung Self-Rating Depression Scale [41]. For assessment of general quality of life Aachener Life Quality Inventory (ALQI) was used [14]. In patients with global aphasia former studies have found good correlation between patient and family assessment [14]. Finally, the patients and their families were asked for disease progression, morbidity and quality of life. They were asked how they

would judge the decision of the operation retrospectively and either give "yes, I would agree again" or "no" as possible answers. The family's burden was assessed by the Caregiver Strain Index [28].

Statistics

All numerical data are given as mean ± standard deviation (SD). Differences between the groups (survivors/ non-survivors, left-/right-hemispheric infarctions, operation within/ after 24 hours) were calculated by Mann-Whitney-UTest or Student's tTest. $P < 0.05$ was presumed to be a statistically significant difference. Excel and SPSS programs were used for calculation.

Results

Table 1 shows demographic data of the patients and the characteristics of infarction. The average age of all patients was 49.7 ± 16.5 years (range 17–76). Non-surviving patients with a mean age of 64.5 ± 9.5 years were significantly older than survivors with a mean age of 40.7 ± 12.6 years ($p = 0.006$). Mean NIHSS on admission was 18.0 ± 1.1 points for survivors as well as non-survivors. Three patients received systemic thrombolysis with rtPA in the first three hours after the stroke. Two of the three patients developed intracranial hemorrhage in the following 24 hours. Between the first and third day,

Table 1 Demographic data and information about the infarctions of 18 patients

No.	Age in years	Sex	Side	Localization of the infarction	Cause	Etiology	Latency until arrival	Latency until operation	Follow-up Rankin-Scale
1	29	m	right	co. MCA co. ACA	ACI stenosis	dissection	0,5h	72 Re-OP 113	1
2	43	m	right	co. MCA	ACI stenosis	traumatic dissection	1h	40	3
3	58	m	right	co. MCA	thrombus of cardiac apex	cardiogen embolic	3h	76	3
4	70	m	right	co. MCA part. ACA	ACI stenosis	cardiogen embolic	over night	39	deceased
5	63	f	right	co. MCA co. ACA	Carotis-T occlusion MCA occlusion	cardiogen embolic	over night	64	deceased
6	56	f	left	co. MCA co. PCA	ACI occlusion	unknown	24h	68	deceased
7	43	f	right	part. MCA	PFO	cardiogen embolic	1h	15	1
8	41	m	left	part. MCA	ACI occlusion MCA occlusion	dissection	1h	55	1
9	52	m	left	co. MCA	ACI occlusion	local thrombotic	over night	16	deceased
10	76	m	right	co. MCA	atrial fibrillation	cardiogen embolic	2h	24	deceased
11	53	f	left	co. MCA part. ACA	ACI occlusion	cardiogen embolic	over night	13	5
12	70	m	left	co. MCA	atrial fibrillation	cardiogen embolic	1h	52	deceased
13	18	m	left	co.MCA part. ACA	ACI stenosis	unknown	1h	22	4
14	43	f	right	co. MCA	ACI occlusion	unknown	1h	24	4
15	52	f	left	co. MCA part. ACA	90 % ACI stenosis	local thrombotic	over night	77	4
16	54	m	right	co. MCA part. PCA borderline	ACI occlusion MCA stenosis	dissection	6	17 Re-OP 60	4
17	17	m	left	part. MCA co. ACA	cardiac operation Carotis-T occlusion	cardiogen embolic	over night	17	3
18	57	f	right	co. MCA	atrial fibrillation	cardiogen embolic	over night	13	4

co. MCA, complete infarction of the middle cerebral artery territory; part. ACA, partial infarction of the anterior cerebral artery territory; part. PCA, partial infarction of the posterior cerebral artery territory; ACI, internal carotid artery

clinical deterioration developed as impairment of consciousness (development of coma (n = 4)), anisocoria (n = 11), nausea and vomiting (n = 8), excessive headache (n = 2)). One patient showed extension attacks, one displayed respiratory insufficiency.

Neuroradiological findings

CT characteristics of the patients are shown in Table 2. Midline shift of the septum pellucidum was more pronounced in non-surviving patients (mean 1.28 ± 0.75 cm) than in surviving patients (0.68 ± 0.58 cm), though the difference did not reach significance (p = 0.119). However, a significant difference of the midline shift was found between patients undergoing operation during the first 24 hours after onset (0.51 ± 0.73cm) compared with those having a later operation (1.24 ± 0.41).

Results of Hemicraniectomy

Twelve (67 %) out of eighteen operated patients survived after malignant middle cerebral infarction. Mortality during the first week was 11 % (2 patients). Both patients died from herniation due to non-manageable brain edema. Four patients (22 %) died 6–37 weeks (mean 20.5 weeks) after onset: three due to the medical complications (pneumonia and septic shock) and one patient bled into the necrotic area and ventricular system followed by brain abscess four months after the stroke and two weeks after receiving skull reconstruction with Palacos.

The operation was performed after a mean period of 39.1 ± 24.2 hours (range 13–77) after onset. There was no difference in the time delay between surviving (mean 36.8 hours) and non-surviving patients (mean 42.3 hours) (p = 0.542). Non-lethal complications during the first 2 weeks after surgery included secondary hemorrhagic transformation in two patients, a thin subdural hematoma in four, hygroma in two, and infected ventricle drainage in two patients.

Results of the follow-up examination

All twelve surviving patients were examined 7–26 months (mean 14.2 ± 6.5 months after the stroke). Eleven of the twelve patients, as well as their relatives, retrospectively agreed that the decision to undergo surgery was the correct decision. One patient was severely handicapped and aphasic; his relatives retrospectively disagreed with the decision to operate.

Table 3 shows the results of the follow-up examination: mean NIHSS was 12.0 ± 4.1 points, mean Barthel-Index 61.1 ± 26.1 points (Fig. 1) and mean Rankin-Scale 3.3 ± 1.2. Two patients had been able to go back to work. Using the Zung Self-Rating Depression Scale, six patients were ranked as slightly depressive, one patient as moderately depressive and five patients as not depressive. There was a mean disability of 58.0 ± 22.7 points on the Aachener Life Quality Inventory (Classification: nine increasing subscales with a maximum of 10 points, subscale of cognition with a maximum of 17 points, total points of 107, 107 points correspond to worst result).

The five patients with no or only slight dependency were younger (34.6 ± 11.4 years, range 17–43) than the more severely handicapped patients with a mean age of 47.8 ± 14.0 years (range 18–58). A comparison of the Barthel-Index between patients younger than 45 years (n = 7) and patients older than 45 years (n = 5) shows a significantly better result for the younger group (< 45 years BI 75.0 ± 20.7; > 45 years BI 40.0 ± 22.7; p = 0.026). Surviving patients with a mean age of 40.7 ± 12.6 years were also significantly younger than non-survivors with 64.5 ± 9.2 years (p = 0.006).

Side of infarction

There were ten right- and eight left-sided infarctions; three patients in each group died. On admission two of the eight left-sided infarctions had a Broca aphasia and six had a global aphasia. All patients with left-sided infarctions had right-sided sensomotor hemiplegia. In the follow-up examination two patients displayed good speech expression with deficits in verbal memory, two patients a Broca aphasia with reduced verbal expression but complete understanding. Only one patient remained severely disabled (BI 10) with incomplete global aphasia.

Table 2 Characteristics of preoperative CT scans

CT characteristics	preoperative CCT	
mean delay from onset of symptoms to CCT	35.1 + 23.7 hours	range 10–73 hours
midline shift	0.88 ± 0.69cm	range 0.2–1.5cm
midline shift	14 patients	78 %
loss of the basal cisterns	4 patients	22 %
uncal herniation	3 patients	17 %
enlargement of the ambient cistern and blockade of foramen Monroi	3 patients	17 %

Table 3 Results of follow-up examination of 12 patients

No.	Age in years	NIHSS Sum	Rankin-Scale	Barthel-Index		Walking ability	Living	Time of Follow-up Examination	Zung SDS		Operation-agreement
				Sum	Degree of Disability				Sum	Depression	
1	29	15	1	90	independent, back at work	independent	at home	22 months	44	slight	yes
2	43	15	3	85	slight	independent	at home	26	42	slight	yes
3	58	12	4	55	moderate	able to stand	nursing home	25	44	slight	yes
7	43	3	1	100	independent, back at work	independent	at home	15	32	no	yes
8	41	13	3	75	slight	independent	at home	11	42	slight	yes
11	53	18	5	10	severe	able to stand	nursing home	14	55	moderate	no
13	18	13	4	50	moderate	able to stand	at home	11	41	slight	yes
14	43	14	4	45	moderate	able to stand	at home	11	47	slight	yes
15	52	14	4	60	slight	with help	at home	11	38	no	yes
16	54	13	4	35	moderate	able to stand	at home	9	36	no	yes
17	17	7	3	85	slight	independent	at home	9	24	no	yes
18	57	13	4	50	moderate	able to stand	at home	7	25	no	yes

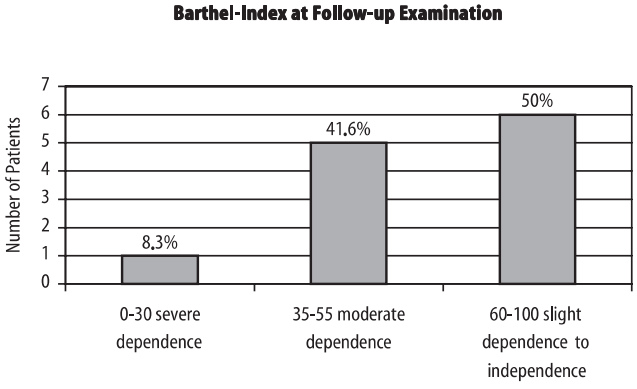

Fig. 1 Barthel-Index 7–26 months after hemicraniectomy in 12 patients

In six out of seven surviving patients with right-hemispheric infarctions we found multimodal neglect syndrome of different degrees. Five patients had a moderate deficit of attention with slow receptivity, problems in task solving, increased distractability and a general disturbance of incentive. In two patients insight and acceptance of the disorder was partially reduced. One patient did not show any deficit except for a left sided hemihypaesthesia.

In the total number of social as well as physical subscales of quality of life there were no significant differences between left- and right-hemispheric infarct patients (68.8 ± 22.3 points left vs. 50.3 ± 21.3 right). ALQI subscale of communication was worse in patients with left hemispheric infarction (5.8 ± 3.6 points vs. 0.6 ± 0.8 points) owing to the aphasia.

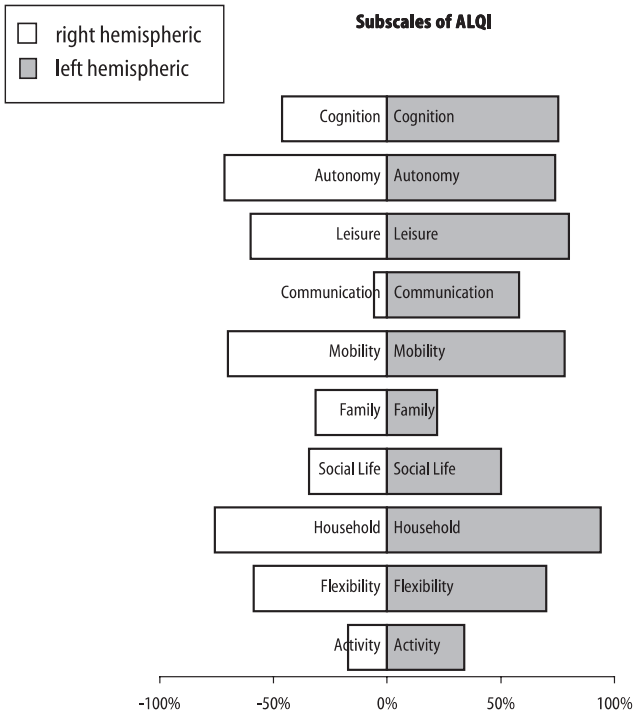

Fig. 2 Subscales of ALQI in patients with right- and left-sided hemicraniectomy after malignant middle cerebral infarction

Discussion

The key question of the present study was whether quality of life during follow-up justified the treatment by

hemicraniectomy in malignant middle cerebral artery infarction. Follow-up examination was performed 7–26 months after hemicraniectomy with a mean of 14.2 ± 6.5 months. All patients were either at home or in a nursing home and were in a stable condition. Even though slight improvement of some functions can not be excluded between six months and two years, prognosis and functional status is not believed to change drastically later than three months after stroke according to the Copenhagen Stroke Study [22]. Health status and quality of life were generally ranked as "satisfactory" in a five-point-scale by the patients. None of the patients was in a vegetative state. Mean Barthel-Index was 61.1 ± 26.1 points. Two patients were totally independent (BI 100 and 90) and were able to go back to work. Four patients (BI 60, 75, 85, 85) were slightly and five patients (BI 35–55) moderately dependent on external assistance. Only one patient was severely dependent on others (BI 10).

There are similar data from the literature about the outcome after malignant MCA infarction: Rieke et al. collected historic data of 79 patients having undergone hemicraniectomy after malignant middle cerebral infarction and found a mortality of 30.4 % [27]. Of surviving patients 34.5 % were severely dependent and 65.5 % moderately dependent or independent [6, 16, 17, 26, 27, 31, 32, 38]. Schwab presented data of 46 surviving patients (73 %) after hemicraniectomy: all patients were able to walk and had a mean Barthel-Index of 68.8 points [34]. In contrast, conservatively treated patients had a mortality of 78 % (43 of 55 patients), twelve surviving patients displayed a mean Barthel-Index of 60.0 points [9] Holtkamp et al. found poor functional outcome in elderly patients with malignant middle cerebral infarction (in both groups Barthel-Index ≤ 60 points, Rankin-Scale = 4); mortality differed between conservatively and operatively treated patients (66 % versus 17 %) [13]. In a study of Carter et al. eight patients had a Barthel-Index better than 60 points (72 %) while three patients were severely dependent (28 %) [4]. In our study, 18 patients had hemicraniectomy, six of whom died (33 %). Our results of follow-up examinations show similar outcome to those found in the other studies (50 % mild, 42 % moderate and 8 % severe disability).

There were a number of complications after surgery in our patients, most of which, however, were not attributable to surgery per se. Early deaths within the first week (n = 2) were due to space occupying lesions too severe to be managed by dural augmentation and craniectomy. All of the other deaths were more than six weeks after surgery, a time period which was less thouroughly studied in previous publications. Medical complications with pneumonia and sepsis accounted for 3 of these later deaths. One patient who died 4 months after surgery and two weeks after Palacos reconstruction of the bone defect had a brain abscess and might be considered the only serious adverse effect directly related to surgery in this series. Non-lethal complications included secondary hemorrhagic transformation of the infarcted area, small subdural hematomas or hygromas and infected ventricular drainages, which all were managed conservatively.

This is the first study looking at detailed data of quality of life after hemicraniectomy. Using Aachener Life Quality Inventory with a maximum of 107 points (corresponding to maximal disability) only a moderate loss of quality of life was found (58.0 ± 22.7 points).

Surprisingly, in our study psycho-social disability was judged much better than expected even though some patients had severe physical and cognitive disorders. The major influence could be attributed to the familial environment. Data from Carter and Rieke also mention good reintegration into the family after hemicraniectomy [4, 27]. A comparison of the results of rehabilitation scales showed good correlation between Barthel-Index as well as NIHSS and the total ALQI score and its physical subscales [4]. However, psycho-social subscales rating "familial interaction", "cognition" and "communication" did not correlate with NIHSS in our patients. Williams et al. also showed that a stroke-specific quality of life scale did not correlate with clinically used scales like the NIHSS and Barthel-Index [39].

Outcome is believed to depend on the side of infarction. Lesions of the dominant hemisphere are associated with global aphasia, apraxia and right sided hemiplegia. Because of expectation of a bad outcome some hemicraniectomy studies have excluded patients affected by left-sided infarctions and complete aphasia [4, 6, 27].

In the trials performed by Schwab et al. there were eleven patients with ischemia of the left hemisphere [27, 33, 34]. One patient died, one did not show any neurological deficit at all; the other nine patients had expressive deficits while understanding and communication recovered. Similarly, de Haan did not find any correlation between side localization and quality of life six month after ischemic stroke in 441 patients who were treated conservatively [5]. Our results did not show any significant differences of life quality assessed by NIHSS, Barthel-Index, Rankin-Scale and ALQI between left and right side hemicraniectomy.

Right-sided lesions may lead to cognitive, emotional and verbal disorders such as deficits of awareness, multimodal neglect syndromes with sublimation of the affected side up to anosognosia and complete denial of the deficit, flattening of emotion, agitation, confusion and reduced cognitive abilities [37]. Even though the ALQI subscale of communication showed a significantly better outcome for patients with a right-sided lesion (0.6 ± 0.8 versus 5.8 ± 3.6), there were no differences between right-sided and left-sided strokes comparing total ALQI. Taken together, our results support hemicraniectomy on either side. The general outcome is

independent of the affected side and hemicraniectomy should not be restricted to right-sided strokes only.

The outcome was related to age but not to side of infarction, time of hemicraniectomy or initial NIHSS. Initial Rankin-Scale (4.9 ± 0.3) and NIHSS (18.0 ± 2.8) were poor but our follow-up data revealed that all but one patients had a relatively good outcome including objective criteria (mean Rankin 3.3 ± 1.2, Barthel-Index 61.1 ± 26.1) as well as subjective criteria (general health state ranking of 3 = "satisfactory" in a 5 point scale).

Depression is a common emotional disorder after stroke, especially in patients with left-sided lesions of the frontal areas or basal ganglia [29]. Using the Self-Rating Depression Scale of Zung, we found mild depression in six patients and a moderate depressive disorder in one patient [41]. Carter found mild depression in nine out of 11 patients [4]. Diagnosis and therapy of a depressive disorder has a major influence on rehabilitation. Parik et al. were able to show that non-depressive patients had a better functional and cognitive outcome than patients with depressive disorders [24].

In the published studies of hemicraniectomy after malignant middle cerebral infarction the burden of family members due to the handicap and disability of the partner was not studied. Relatives and family members gave about as many times the answer "burdened" (mean of 5.1 times) as "non burdened" (mean of 5.5 times) in the twelve questions of the Caregiver Strain Index. The complaints centered on the physical, emotional, economical and familial changes due to the patients disability after the stroke. A French study found similar results with a "10-cm visual analog scale" rating the burden of family members 17.6 months after the event with a mean value of "4.9cm" [2]. In our study there was a surprising difference between the medical and functional results of rehabilitation (measured with Barthel-Index and NIHSS) and the personal satisfaction with the outcome: some family members thought themselves to be only slightly burdened although the support for the partner or parent required a lot of time or family changes. On the other hand, we found negative responses from patients who had an objectively excellent rehabilitative outcome. Even if there is no statistical relevance in these findings it shows that quality of life is dependent not only on the disability, but also surrounding factors such as premorbid style of living and the personality of the patient and his relatives [20].

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