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JOURNAL OF THE AMERICAN HEART ASSOCIATION

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*Stroke* 2004;35;539-543; originally published online Jan 5, 2004;

DOI: 10.1161/01.STR.0000109772.64650.18

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75214

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ISSN: 1524-4628

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# Hemicraniectomy for Massive Middle Cerebral Artery Territory Infarction

## A Systematic Review

Rishi Gupta, MD; E. Sander Connolly, MD; Stephan Mayer, MD; Mitchell S.V. Elkind, MS, MD

**Background and Purpose**—Hemicraniectomy and durotomy have been proposed in many small series to relieve intracranial hypertension and tissue shifts in patients with large hemispheric infarcts, thereby preventing death from herniation. Our objective was to review the literature to identify patients most likely to benefit from hemicraniectomy.

**Methods**—All available individual cases from the English literature were reviewed and analyzed to determine whether age, vascular territory of infarction, side of infarction, reported time to surgery, and signs of herniation predict outcome in patients after hemicraniectomy. All studies included were retrospective and uncontrolled; there were no randomized controlled trials.

**Results**—Of 15 studies screened, 12 studies describing 129 patients met the criteria for analysis; 9 patients treated at our institution were added, for a total of 138 patients. After a minimum follow-up of 4 months, 10 patients (7%) were functionally independent, 48 (35%) were mildly to moderately disabled, and 80 (58%) died or were severely disabled. Of 75 patients who were >50 years of age, 80% were dead or severely disabled compared with 32% of 63 patients ≤50 years of age ( $P<0.00001$ ). The timing of surgery, hemisphere infarcted, presence of signs of herniation before surgery, and involvement of other vascular territories did not significantly affect outcome.

**Conclusions**—Age may be a crucial factor in predicting functional outcome after hemicraniectomy in patients with large middle cerebral artery territory infarction. (*Stroke*. 2004;35:539-543.)

**Key words:** craniectomy ■ emergency treatment ■ stroke ■ surgical treatment

Stroke is the second-leading cause of death worldwide.<sup>1</sup> Up to 10% of ischemic strokes may be characterized as massive hemispheric or malignant space-occupying supratentorial infarcts.<sup>2</sup> These patients often present with hemiplegia, forced head and eye deviation, aphasia, or a contralateral neglect syndrome. They experience progressive decline in level of consciousness typically over 48 hours, ultimately succumbing as a result of transtentorial herniation within 48 to 96 hours. Despite medical treatments such as hyperventilation, mannitol, barbiturate coma, and hypothermia, mortality is estimated to be between 50% and 78%.<sup>3</sup>

Decompressive surgery was first reported as a potential treatment for large hemispheric infarction in case reports as early as 1956. The procedure involves removal of a generous bone flap (frontotemporal-parietal) ipsilateral to the side of the infarction, followed by opening of the dura to allow outward herniation of the brain. This would thereby reduce the intracranial pressure and prevent downward herniation.<sup>4</sup>

Since that time, several case series or case reports have reported improved survival of patients after craniectomy, but no definitive conclusion has been reached as to any benefit in

functional outcomes.<sup>5-20</sup> The largest case series<sup>5</sup> suggested that early decompression (ie, <24 hours) reduces mortality and may provide improved outcomes by avoiding the consequences of brainstem compression from transtentorial herniation. Patients who underwent early hemicraniectomy had a mortality rate of 16% compared with 34% for delayed surgery. They postulated that waiting for signs of herniation may worsen prognosis because of irreversible mesencephalic injury.<sup>5</sup>

Here, we present an analysis of the individual patients reported in the literature and our institution with the goal of identifying patients who are more likely to benefit from decompression. Because no randomized control studies are currently published in the literature, we analyzed individual data from retrospective and uncontrolled case series. Although a formal meta-analysis could not be performed with the available data, this approach may provide insight into which patients may benefit from the procedure.

## Subjects and Methods

### Search Strategy

We performed a MEDLINE search of English language literature from 1970 on using the keywords *hemicraniectomy*, *decompressive*

Received April 28, 2003; final revision received July 22, 2003; accepted October 1, 2003.

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Stroke is available at <http://www.strokeaha.org>

DOI: 10.1161/01.STR.0000109772.64650.18

TABLE 1. Distribution of Outcomes Based on Possible Predictors

	n	Functional Independence, n (%)	Mild to Moderate Disability, n (%)	Severe Disability, n (%)	Death, n (%)
Age range (n=138), y					
11–30	15	5 (33)	7 (47)	2 (13)	1 (7)
31–50	48	4 (8)	27 (56)	9 (19)	8 (17)
≥51	75	1 (1)	14 (19)	36 (48)	24 (32)
Side infarcted (n=138)					
Left	27	1 (4)	10 (37)	9 (33)	7 (26)
Right	111	9 (8)	38 (34)	38 (34)	26 (24)
Time to surgery (n=131), h					
0–24	45	3 (7)	14 (31)	15 (33)	13 (29)
25–48	35	1 (3)	15 (43)	9 (26)	10 (29)
49–72	18	1 (6)	6 (33)	6 (33)	5 (28)
≥73	33	5 (15)	11 (33)	13 (39)	4 (12)
Vascular territory (n=129)					
MCA	88	6 (7)	30 (34)	30 (34)	22 (25)
MCA+ACA or PCA	41	2 (5)	16 (39)	13 (32)	10 (24)

ACA indicates anterior cerebral artery; PCA, posterior cerebral artery.

*craniectomy*, and *decompressive surgery* in various combinations with the keywords *stroke*, *middle cerebral artery infarct*, and *malignant cerebral infarct*. The bibliographies of all identified studies were searched for additional references; this method was repeated until no further studies were found.

### Study Eligibility

Patients were selected from case reports, case series, and our institution (Columbia-Presbyterian Medical Center) if they underwent a hemispheric resection for a middle cerebral artery (MCA) territory infarct or MCA plus another vascular territory infarct (ie, anterior cerebral and/or posterior cerebral arteries) after 1970. These patients were included if the authors reported age, side of infarct, and a functional outcome score (Barthel Index [BI], modified Rankin Scale [mRS], Glasgow Outcome Scale [GOS], or clinical description) at least 4 months after the procedure. Patients within a case series who underwent decompressive surgery for reasons other than MCA infarction were excluded.

### Data Extraction

These articles were reviewed and data were extracted by means of a standardized data extraction form. Data collected by 1 of the authors (R.G.) included age and sex of the patient, vascular territories and side of the infarction, origin of stroke, time to surgery, presence of preoperative signs of clinical herniation (pupillary dilatation or bilateral motor posturing), whether the patient or their proxy would have elected to have the surgery again based on their current outcome, and functional outcome based on the BI, mRS, GOS, or clinical description.

Reported outcomes were classified into 4 specific categories: (1) functionally independent (BI ≥90; mRS, 0 to 1; or GOS, 5); (2) mild to moderate disability (BI, 60 to 85; mRS, 2 to 3; or GOS, 4); (3) severely disabled (BI <60; mRS, 4 or 5; or GOS, 2 to 3); or (4) death. Because of the lack of consensus for defining outcomes with activity of daily living scales, comparing various studies may be difficult. After a review of several acute stroke trials, Sulter et al<sup>21</sup> suggested that it may be preferable to dichotomize outcomes by defining poor outcomes as BI <60, mRS >3, death, or placement in an institution. We dichotomized the data into good and poor outcomes as such. Good outcomes were defined as functionally independent or mild to moderate disability. Poor outcomes were defined as severe disability or death. Thirteen patients were not

assigned a functional outcome score by the original authors, two of whom were difficult to categorize. Thus, 11 patients, for whom a clinical description of functional status was given, were reviewed and assigned to a category by 2 authors (R.G. and M.S.E.) using the following criteria: (1) able to ambulate without assistance and to perform all their usual duties (functionally independent); (2) able to ambulate without assistance but unable to perform previous activities (mild to moderate disability); or (3) bed bound or requiring maximal assistance (severely disabled). Agreement occurred in 91% of cases. If disagreement occurred, consensus was reached after discussion.

### Statistical Analysis

All data accumulated from the literature and from the patients from our institution were equally weighted and pooled. SPSS 10.0 was used to analyze the database. A univariate analysis was performed, and dichotomous variables were compared with the Pearson's  $\chi^2$  test. Differences were considered significant at  $P < 0.05$ . In the multivariate logistic regression model, statistical significance was also considered at  $P < 0.05$ . Age was the only variable found to be significant in the multivariate model.

### Results

There were 129 patients in the literature and 9 patients from our institution for whom individual data on patient age, side of infarct, and functional outcomes were available. The results are summarized in Tables 1 and 2. Seventy-four patients from 3 studies were excluded because individual patient data were not available for analysis (Table 3). The mean age of the patients analyzed was 50 years (range, 11 to 76 years); 74 (53%) were men; and the overall mean time to surgery was 59.3 hours (range, 8 to 456 hours). Of these patients, 58 (42%) had good outcomes, while 80 (58%) had poor outcomes. The overall mortality rate was 24%.

Data for time to surgery, vascular territory involved, and presence of herniation signs were not available for 7, 9, and 56 patients, respectively. The available data were equally weighted and pooled for the analysis.

Of the 75 patients >50 years of age, 60 (80%) were dead or severely disabled, which was significantly higher than the

**TABLE 2. Summary of Case Series With Individual Patient Data Used in the Analysis**

Author	Right MCA, n	Left MCA, n	Mean Age, y	Patients With Early Surgery, n (%)	Patients With Brainstem Signs, n (%)	Mean Time to Follow-Up, mo	Patients With Good Outcome, n (%)	Patients Died, n (%)	Patients Who Would Consider the Same Surgery/Survived, n
Carter et al <sup>8</sup>	14	0	49	5 (36)	14 (100)	12	8 (57)	3 (21)	6/11
Walz et al <sup>7</sup>	10	8	50	9 (50)	NA	14	6 (33)	6 (33)	11/12
Leonhardt et al <sup>10</sup>	26	0	50	11 (42)	NA	12	11 (42)	6 (23)	14/20
Holtkamp et al <sup>6</sup>	9	3	65	4 (33)	0 (0)	7	1 (8)	4 (33)	NA
Delashaw et al <sup>20</sup>	9	0	57	3 (33)	7 (78)	15	4 (44)	1 (11)	8/9
Rieke et al <sup>14</sup>	26	6	49	8 (25)	24 (75)	13	16 (50)	11 (34)	NA
Koh et al <sup>12</sup>	4	3	45	NA	NA	7	2 (29)	1 (14)	NA
Rengachary et al <sup>16</sup>	3	0	31	0	3 (100)	21	1 (33)	0 (0)	NA
Kalia and Yonas <sup>15</sup>	2	2	34	1 (25)	2 (50)	17	3 (75)	0 (0)	2/4
Young et al <sup>19</sup>	1	0	59	0 (0)	1 (100)	9	0 (0)	0 (0)	NA
Ivamoto et al <sup>18</sup>	1	0	49	0	1 (100)	7	1 (100)	0 (0)	NA
Kondziolka et al <sup>17</sup>	3	1	42	2 (50)	4 (100)	20	4 (100)	0 (0)	NA
Our institution	5	4	53	2 (22)	6 (66)	8	1 (11)	1 (13)	3/8

20 of 63 (32%) of those ≤50 years of age who had poor outcomes ( $P<0.00001$ ). The mortality rate was also significantly higher (32%, 24 of 75 patients) for those >50 years of age compared with 14% (9 of 63 patients) for those ≤50 years of age ( $P<0.012$ ).

There were 131 patients for whom time to surgery and functional outcomes were documented. Of the 45 patients (mean age, 48.6 years) who underwent hemicraniectomy within 24 hours (mean, 20.5 hours), 17 (38%) had a good outcome, and 28 (62%) were severely disabled or dead at follow-up. There were 51 patients (mean age, 51.7 years) who had decompression after 48 hours (mean, 106 hours): 23 (45%) had a good outcome, and 28 (55%) had bad outcomes. There was no significant difference between the 2 groups.

Presence of signs of herniation before surgery was available in only 82 (59%) of patients analyzed; 63 had signs of herniation before decompression. Thirty-three of these patients (52%) were independent or mildly to moderately disabled, whereas 6 of the 19 patients (32%) who underwent surgery before signs of brainstem compression had good outcomes. There was no statistically significant difference between the 2 groups ( $P<0.12$ ).

Comparison of MCA territory infarcts with MCA plus involvement of other territories was not statistically significant. Hemicraniectomy on the left side did not show a statistical difference compared with the right side. Patients

undergoing decompression of the dominant hemisphere were younger (45 versus 51 years of age).

**Discussion**

Decompressive surgery has been studied as a way to relieve the mass effect and tissue shifts related to mass lesions. Hemicraniectomy and durotomy can relieve the pressure from swollen, infarcted brain tissue, preventing brain herniation and death. This method has been tested in models of stroke in rats<sup>22</sup> and in anecdotal reports and comparison studies in humans.<sup>4-20</sup> In our analysis of the published cases, younger patients had better functional outcomes, whereas the hemisphere infarcted and presence of signs of herniation did not seem to affect outcomes.

Although mortality rates probably fall after decompressive surgery,<sup>14</sup> it is unclear which groups of patients benefit most from the procedure. In addition, the issue of quality of life after hemicraniectomy has been controversial, with concerns about leaving patients with severe deficits that may not be accounted for by the BI, mRS, or GOS.<sup>7,10</sup>

There has been interest in identifying which patients will develop malignant cerebral edema after massive infarcts.<sup>9</sup> Identification of patients at high risk of malignant edema might allow earlier and potentially more effective intervention in select cases. Radiographic and clinical signs such as early hypodensity of >50% of the MCA territory, early

**TABLE 3. Summary of Large Case Series Without Individual Data for Analysis**

Author	Right MCA, n	Left MCA, n	Mean Age, y	Mean Time to Surgery, h	Brainstem Signs, n (%)	Mean Time to Follow-Up, mo	Average BI of Survivors	Patients With Good Outcome, n (%)	Deaths, n (%)
Hacke et al <sup>2*</sup>	21	34	56	...	45 (82)	1	60	...	43 (78)
Schwab et al <sup>5</sup>	26	5	50.3	21	4 (13)	3	68.8	26 (84)	5 (16)
Sakai et al <sup>11</sup>	13	11	63.6	94	18 (75)	2	...	0 (0)	8 (33)
Mori et al <sup>9</sup>	14	5	67	...	...	3	28	4 (21)	3 (16)

\*Patients treated with maximal medical therapy (no decompressive surgery).

nausea or vomiting, and a National Institutes of Health Stroke Scale score  $\geq 20$  for left or  $\geq 15$  for right hemisphere MCA infarction may predict which patients will develop malignant edema.<sup>23</sup> More recently, a broad-based population was studied, and hypertension, heart failure, elevated white blood cell counts, and involvement of additional vascular territories were also associated with an increased risk of fatal brain swelling.<sup>24</sup> Early hemicraniectomy based on radiographic and clinical criteria, but before signs of brain stem herniation, has been proposed as a means of improving outcomes.<sup>5</sup>

Animal and clinical studies have provided evidence for a benefit of early surgery. In a rat MCA occlusion model, hemicraniectomy markedly reduced mortality. Even more intriguing, though, was the finding that hemicraniectomy reduced the volume of infarcted brain tissue, and that early decompression (ie, at 1 versus 24 hours) reduced infarct volume to a greater extent.<sup>22</sup> Schwab et al<sup>5</sup> presented the most convincing data for the benefits of early decompression in patients without signs of herniation. In their series, only 4 of the 31 patients (13%) who underwent early decompression had signs of herniation at the time of surgery (mean time to surgery, 21 hours). Of these 31, 26 (84%) had a BI  $>60$  at follow up. Our analysis of the published cases, however, did not show benefit to early surgery ( $<24$  hours), but a greater proportion of patients (64%) had signs of herniation before surgery. Moreover, of the 45 patients undergoing early surgery, data for signs of herniation were available for only 25 patients. We found no impact of signs of herniation at the time of surgery on outcomes. This may be explained by early reversal through medical and surgical treatment. A single herniation event without radiographic evidence of midbrain injury may not prohibit a good long-term outcome.<sup>25</sup> On the other hand, the missing data for a large proportion of patients in the literature may have biased our results.

The impact of age on outcome has not been well studied in large hemispheric stroke. There are reports of poor functional outcomes and increased mortality in older patients who undergo hemicraniectomy.<sup>6-8,12</sup> This is in concordance with what we found in our systematic review. Older age may have an effect on the ability of the brain to compensate from a stroke. In addition, older patients tend to have comorbid conditions that likely increase the risk of poor outcomes and mortality. Conversely, younger patients may be expected to have better outcomes, but a lack of cerebral atrophy may not allow them to tolerate massive edema as in older patients. This was used to justify early hemicraniectomy in the younger population in some studies.<sup>8,14</sup> Wijdicks and Diringer<sup>26</sup> studied the natural history of 42 patients with MCA territory infarction, of whom 33 demonstrated increased drowsiness, progressive diencephalic herniation, or uncal herniation. Interestingly, of the 11 patients  $<45$  years of age, 3 died (28%), whereas the mortality rate for patients  $>45$  years of age was 90.9% (20 of 22 patients). Functional status of the 8 survivors was not described, but the study provides evidence that younger patients may have a better prognosis than older patients. Our review of the literature supports these observations in younger patients who have a better outcome after decompressive surgery. Nine of 63 patients (14%)  $<50$  years of age died despite surgery com-

pared with 24 of 75 patients (32%)  $>50$  years of age. Age may be the most important factor in deciding which patients should undergo hemicraniectomy.

Offering life-saving treatment for large dominant-hemisphere infarcts is controversial. The major concern has been that heroic interventions may leave patients with an unacceptably poor quality of life because of aphasia.<sup>8</sup> Data from our review of the literature, however, do not support an absolutist approach to treatment of only the nondominant hemisphere. Among the 27 patients who had decompression of the dominant hemisphere, functional outcome was no worse than among the 111 patients who had nondominant infarcts. There are several explanations for the lack of difference between the hemispheres. First, the patients were younger and fewer in the dominant hemisphere group. Second, language deficits may be of small consequence in patients who are severely disabled by hemiplegia. Third, nondominant hemisphere strokes can lead to severe depressive, abulic, or neglect states that may interfere with rehabilitation efforts and are as disabling as aphasia.<sup>7</sup> Fourth, global disability scales such as the BI, mRS, and GOS may emphasize mobility as opposed to language dysfunction. Finally, our understanding of what patients view as acceptable outcomes may be poor. Assessments of patients at risk of stroke have shown that severe disabling hemiplegia is often viewed as worse than aphasia or death.<sup>27</sup> This suggests that infarction side should not necessarily be an exclusion criterion for surgery.

Hemicraniectomy reduces mortality in patients with malignant MCA syndromes, but it is not clear which patients may avoid severe disability after the procedure. Younger patients may have better functional outcomes after surgery, but we still do not have a good understanding of the natural history of the disease in this subgroup. The overall mortality rate (24%) was lower in our review of patients who underwent hemicraniectomy compared with reports as high as 78%<sup>2</sup> for the natural progression of the disease. In addition, a good proportion of patients reviewed (58 of 138, 42%) had good outcomes after decompressive surgery. A large number of patients or proxies (45 of 64, 70%) stated that they would undergo the procedure again if posed with the same situation. Such observations justify further study of hemicraniectomy as a potential treatment of large MCA territory infarctions.

There are several limitations to our review. The individual data analyzed were obtained from uncontrolled, retrospective data; thus, formal meta-analysis techniques could not be applied. Such an analysis cannot control for data heterogeneity, which limits the scope of this study. The patients reviewed also lacked a uniform approach and follow-up time. In addition, all data were not always provided for all cases, and 13 of the 138 patients (9%) were assigned a functional category on the basis of clinical descriptions provided in the literature. Publication bias may also exist within the literature, with an overrepresentation of patients with good outcome.

Although there are limitations to this approach, it may provide some useful hypotheses for future clinical trials. Age may be the most important factor when deciding on surgery, whereas laterality and additional vascular territory involve-

ment may not affect outcomes. There are 2 ongoing prospective clinical trials looking at early decompression as a means of improving functional outcomes.<sup>28,29</sup> Future trials or standardized protocols may consider focusing on hemicraniectomy in younger patients or early surgery before signs of herniation.

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