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Hemicraniectomy in Older Patients with Extensive Middle-Cerebral-Artery Stroke

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ABSTRACT

BACKGROUND

Early decompressive hemicraniectomy reduces mortality without increasing the risk of very severe disability among patients 60 years of age or younger with complete or subtotal space-occupying middle-cerebral-artery infarction. Its benefit in older patients is uncertain.

METHODS

We randomly assigned 112 patients 61 years of age or older (median, 70 years; range, 61 to 82) with malignant middle-cerebral-artery infarction to either conservative treatment in the intensive care unit (the control group) or hemicraniectomy (the hemicraniectomy group); assignments were made within 48 hours after the onset of symptoms. The primary end point was survival without severe disability (defined by a score of 0 to 4 on the modified Rankin scale, which ranges from 0 [no symptoms] to 6 [death]) 6 months after randomization.

RESULTS

Hemicraniectomy improved the primary outcome; the proportion of patients who survived without severe disability was 38% in the hemicraniectomy group, as compared with 18% in the control group (odds ratio, 2.91; 95% confidence interval, 1.06 to 7.49; P=0.04). This difference resulted from lower mortality in the surgery group (33% vs. 70%). No patients had a modified Rankin scale score of 0 to 2 (survival with no disability or slight disability); 7% of patients in the surgery group and 3% of patients in the control group had a score of 3 (moderate disability); 32% and 15%, respectively, had a score of 4 (moderately severe disability [requirement for assistance with most bodily needs]); and 28% and 13%, respectively, had a score of 5 (severe disability). Infections were more frequent in the hemicraniectomy group, and herniation was more frequent in the control group.

CONCLUSIONS

Hemicraniectomy increased survival without severe disability among patients 61 years of age or older with a malignant middle-cerebral-artery infarction. The majority of survivors required assistance with most bodily needs. (Funded by the Deutsche Forschungsgemeinschaft; DESTINY II Current Controlled Trials number, ISRCTN21702227.)

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Large space-occupying middle-cerebral-artery or hemispheric ischemic brain infarcts are associated with the development of massive brain edema, which may lead to herniation and early death. This condition, which has been described as malignant middle-cerebral-artery infarction, is associated with 80% mortality due to herniation during the first week, despite maximal conservative treatment in the intensive care unit (ICU), including osmotherapy, barbiturates, and hyperventilation.[1-8] Conservative therapies for ischemic brain edema are not supported by sufficient evidence from clinical trials.[9,10]

Decompressive hemicraniectomy (temporary removal of a large part of the skull) combined with duraplasty allows edematous tissue to expand outside the neurocranium, thereby preventing fatal internal displacement of brain tissue and subsequent herniation.[9] A pooled analysis of three randomized, controlled trials has shown the benefit of hemicraniectomy in patients with a malignant middle-cerebral-artery infarct.[5-8] Early hemicraniectomy (i.e., within 48 hours after the onset of stroke) increased 1-year survival from 29% to 78%. The rate of survival with severe disability was low in both groups (4% in the hemicraniectomy group and 5% in the control group). Forty-three percent of patients who underwent hemicraniectomy had a relatively good outcome (survival with mild or moderate disability), as compared with 21% of patients who received conservative treatment.[5]

The upper age limit in this pooled analysis was 60 years. In older patients, the benefit of decompressive hemicraniectomy is uncertain. Observational data suggest that the treatment effect may be smaller in older patients who undergo hemicraniectomy than in younger patients.[11] In a study by Uhl et al.,[12] 12% of patients older than 50 years of age who underwent hemicraniectomy survived with functional independence, whereas 37% died or were severely disabled. Gupta et al.[13] reported that 80% of patients older than 50 years of age who underwent hemicraniectomy were severely disabled or died. In the Decompressive Surgery for the Treatment of Malignant Infarction of the Middle Cerebral Artery II (DESTINY II) study, we investigated the outcome of early hemicraniectomy as compared with conservative treatment in the ICU alone in patients 61 years of age or older with malignant middle-cerebral-artery infarction.

Methods

Design

In this prospective, randomized, controlled, open, multicenter trial, we randomly assigned patients, in a 1:1 ratio, to treatment in the ICU alone (the control group) or early hemicraniectomy (the hemicraniectomy group). Randomization was performed with the use of an online tool (www.randomizer.at) within 48 hours after the onset of symptoms.

This investigator-initiated trial was sponsored by the German Research Foundation. It was approved by the institutional review boards of the University Hospital of Heidelberg and of all participating centers. DESTINY II was conducted at 13 German sites between August 2009 and May 2013. All patients or their legally authorized representatives provided written informed consent.

The study was designed by the steering committee and two of the authors. All the authors had full access to the data and vouch for the completeness and accuracy of the data; there was no writing assistance from anyone who is not listed as an author. There was no commercial support for this study. The published trial protocol includes details of randomization, a complete list of inclusion and exclusion criteria, details of the surgical and control treatments, and the statistical analysis plan.[14] The protocol is also available with the full text of this article at NEJM.org.

Patients

Patients were eligible for inclusion in the study if they were 61 years of age or older, had clinical symptoms of acute unilateral middle-cerebral-artery infarction with an onset of symptoms less than 48 hours before the initiation of treatment, and had scores higher than 14 (in patients with an infarction in the nondominant hemisphere) or higher than 19 (in patients with an infarction in the dominant hemisphere) with reduced levels of consciousness on the National Institutes of Health Stroke Scale (NIHSS) (total scores on the NIHSS range from 0 to 42, with higher scores indicating more severe stroke). An additional criterion for inclusion was ischemic infarction of at least two thirds of the middle-cerebral-artery territory, including the basal ganglia, on brain imaging.

Exclusion criteria were a preexisting score of more than 1 on the modified Rankin scale (on a scale of 0 to 6, with 0 indicating no symptoms

and 6 indicating death) or a preexisting score of less than 95 on the Barthel index of functional levels in activities of daily living (on a scale ranging from 0 [complete dependence] to 100 [independence] in increments of 5). Additional exclusion criteria were the absence of pupillary reflexes, a score of less than 6 on the Glasgow Coma Scale (on which scores range from 3 to 15, with lower scores indicating reduced levels of consciousness), hemorrhages or other associated brain lesions, contraindications to surgery, or an estimated life expectancy of less than 3 years.

TREATMENT

Treatment was initiated within 48 hours after the onset of symptoms and not later than 6 hours after randomization. Conservative treatment options, based on a consensus protocol used by all participating centers, included basic therapy in the ICU for stroke; osmotherapy with the use of mannitol, glycerol, or hypertonic hydroxyethyl starch; sedation; intubation and mechanical ventilation; hyperventilation; and administration of buffer solutions. Surgical treatment consisted of a large hemicraniectomy (with a diameter of at least 12 cm) and duroplasty. The surgical standards and the conservative treatment protocol are detailed in the study protocol.[14]

OUTCOMES AND END POINTS

Data were collected during hospitalization and at two follow-up visits scheduled 6 months (plus or minus 14 days) and 12 months (plus or minus 14 days) after randomization. Follow-up assessment was performed by study physicians who were otherwise not involved in the trial or treatment of the patients. The primary outcome was a score of 0 to 4 on the modified Rankin scale at 6 months. Secondary end points, assessed 12 months after randomization, included the survival rate, the NIHSS score, the score on the modified Rankin scale, the level of activities of daily living (according to the Barthel index), quality of life as measured by means of the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) (with scores ranging from 0 [severely affected] to 100 [not affected]) and the EuroQoL Group 5-Dimension Self-Report Questionnaire (EQ-5D) visual-analogue scale (with scores ranging from 0 [worst] to 100 [best]), the level of depression according to the Hamilton Depression Rating Scale (HDRS) (with scores ranging from 0 to 52 and scores >19 indicating severe depression), and adverse events, including surgical complications. Patients or their caregivers (if patients were unable to understand the question because of severe cognitive impairment or aphasia) were also asked the question "Do you, in retrospect, consent to the treatment you received?"

STATISTICAL ANALYSIS

DESTINY II was designed as a sequential trial to stop recruitment as soon as harm, futility, or efficacy was shown, with the use of an overall two-sided significance level of 5% in the analysis of the primary end point. Sequential interim analyses were performed according to prespecified rules with the use of Whitehead's triangular test for binary outcomes (PEST software, version 4.4) each time a patient reached the primary end point.[15,16] The result is reported as an odds ratio with a bias-corrected 95% confidence interval, adjusted for the sequential nature of the trial.[15-17] The sample size was determined for 90% power, assuming success rates of 31.0% (in the hemicraniectomy group) and 8.6% (in the control group); these rates correspond to a log odds ratio of 1.56.

In each interim analysis, the preliminary data set included data from all patients for whom complete end-point information was available, and the triangular test was performed on the log odds ratio. As soon as an interim analysis showed a significant difference in success rates or the criterion for stopping for futility was reached, the data and safety monitoring board was informed, and the steering committee was asked to stop the trial if that was the board's recommendation. It was assumed that at that time, additional patients had already undergone randomization but had not yet reached the 6-month assessment of the primary end point. The confirmatory analysis is based on all patients who underwent randomization (the intention-to-treat population). The findings of the sensitivity analyses are reported in the Supplementary Appendix (available at NEJM.org) for the preliminary data set and the per-protocol data set, which excluded data from 11 patients with major protocol violations (i.e., crossover and delayed end-point assessment), as well as for the modified Rankin scores, dichotomized as 0 to 3 versus 4 to 6, and the raw modified Rankin scores.[18] All results for secondary end points refer to the intention-to-treat population evalu-

ated 12 months after stroke. Summary statistics are reported as raw frequencies. Tests of group differences were made with standard methods (chi-square test, Wilcoxon rank-sum test, or log-rank test, depending on the type of variable). Group comparisons were based on data on the survivors and on the intention-to-treat population, with a worst-case assumption for missing end points in patients who had died and, for patients with an unknown modified Rankin score or NIHSS score, imputation of the last known observation after randomization (last observation carried forward, or 6-month results for the modified Rankin scale).

RESULTS

STUDY PATIENTS

Between August 2009 and March 2012, a total of 112 patients were randomly assigned to a study group. Baseline demographic and clinical characteristics of the patients are shown in Table 1. Figure S1 in the Supplementary Appendix shows randomization, treatment, and outcomes. Patient recruitment was stopped on the recommendation of the data and safety monitoring board after 82 patients (40 patients in the hemicraniectomy group and 42 patients in the control group) had been assessed for the primary end point at 6 months (Fig. S2 in the Supplementary Appendix). At that time, a total of 30 additional patients (9 patients in the hemicraniectomy group and 21 patients in the control group) had undergone randomization but had not yet reached the 6-month follow-up evaluation.

PRIMARY END POINT AT 6 MONTHS

In the intention-to-treat population (all 112 patients), 20 of 49 patients in the hemicraniectomy group had a score of 4 or better on the modified Rankin scale versus 10 of 63 patients in the control group (bias-corrected estimate of the rate of survival without severe disability, 38% in the hemicraniectomy group and 18% in the control group; odds ratio, 2.91 in favor of hemicraniectomy; 95% confidence interval [CI], 1.06 to 7.49; P=0.04) (Table 2). Whereas the analysis of the raw modified Rankin scores in a sequential proportional-odds model confirmed this result (bias-corrected odds ratio, 3.97; 95% CI, 1.39 to 8.76; P=0.01), on the modified Rankin scale, scores dichotomized as 0 to 3 (survival without moderately severe disability) versus 4 to 6 did not reveal significant effects of hemicraniectomy. Detailed results of all sensitivity analyses are provided in Figures S2 through S5 and Tables S2 and S3 in the Supplementary Appendix.

No patients who survived had a score of 0 to 2 on the modified Rankin scale. Only 7% of patients in the hemicraniectomy group had a score of 3 on the modified Rankin scale, as compared with 3% in the control group. The rates for a score of 4 on the modified Rankin were 32% and 15%, respectively. A score of 5 on the modified Rankin scale was more frequent in the surgery group (28% vs. 13%), whereas death occurred much less frequently in the surgery group (33% vs. 70%) (Fig. 1A).

SECONDARY END POINTS AT 12 MONTHS

The 12-month survival rate was 57% (95% CI, 42 to 72) in the hemicraniectomy group (27 of the 47 patients for whom survival status was known) and 24% (95% CI, 14 to 37) in the control group (15 of the 62 patients for whom survival status was known) (Fig. 2). Table 2 shows the percentages of patients in each group with various scores on the modified Rankin scale. In the intention-to-treat analysis, in which worst values were imputed for patients who had died, all secondary end points (raw modified Rankin score, NIHSS score, Barthel index score, SF-36 score, HDRS score, and EQ-5D score) were significantly better in the hemicraniectomy group. This effect was caused by the large difference in mortality and by the worst-case imputation of missing end points in patients who had died (Table 2). Analyses of secondary end points that excluded patients who had died did not show any significant differences between the groups (Table 2). Among surviving patients, 63% of those in the hemicraniectomy group and 53% of those in the control group gave retrospective consent to treatment (Table S5 in the Supplementary Appendix). The outcome was not influenced by withdrawal of care in either treatment group.

Figure S8 in the Supplementary Appendix shows the SF-36 quality-of-life scores among survivors in DESTINY II, as compared with the average scores in a population of older survivors of mild or moderate stroke and the general population of older persons without stroke.[19,20]

SAFETY

Eighty-eight serious adverse events were reported in the hemicraniectomy group and 84 serious adverse events were reported in the control group

Table 1. Demographic and Clinical Characteristics of the Patients at Baseline.*

Characteristic	Hemicraniectomy Group (N=49)	Control Group (N=63)
Age — yr		
Median	70	70
Range	62–82	61–80
Sex — no. (%)		
Male	25 (51)	31 (49)
Female	24 (49)	32 (51)
Preexisting modified Rankin scale score — no. (%)†		
0	39 (80)	53 (84)
1	10 (20)	10 (16)
2–6	0	0
Preexisting Barthel index score‡		
Median	100	100
Range	95–100	95–100
Site of infarction — no. (%)		
Middle cerebral artery	36 (73)	40 (63)
Middle cerebral artery and anterior cerebral artery	11 (22)	18 (29)
Middle cerebral artery and posterior cerebral artery	2 (4)	5 (8)
Stroke in dominant hemisphere — no. (%)	16 (33)	25 (40)
Glasgow Coma Scale score§		
Median	12	10
Range	6–15	6–15
NIHSS total score¶		
Assessable — no. (%)	34 (69)	39 (62)
Median	20	21
Range	15–40	15–38
Time from onset of symptoms to randomization — hr		
Median	25	26
Range	12–49	9–47
Time from onset of symptoms to hemicraniectomy — hr		
Median	28	NA
Range	16–50	NA
Adherence to assigned treatment — no. (%)	48 (98)	62 (98)
Provision of informed consent — no. (%)		
Patient	7 (14)	5 (8)
Legal representative	12 (24)	12 (19)
Relative, application for legal representation, or independent physician‖	30 (61)	46 (73)

* NA denotes not applicable.
† Scores on the modified Rankin scale range from 0 to 6, with 0 indicating no symptoms, 1 no substantial disability despite the presence of symptoms, 2 slight disability, 3 moderate disability necessitating some help, 4 moderately severe disability, and 5 severe disability; a score of 6 indicates death. Persons with a score of 0, 1, or 2 are considered to be functionally independent.
‡ Scores on the Barthel index range from 0 (complete dependence) to 100 (independence) in increments of 5.
§ Scores on the Glasgow Coma Scale range from 3 to 15, with lower scores indicating reduced levels of consciousness.
¶ Scores on the National Institutes of Health Stroke Scale (NIHSS) range from 0 to 42, with higher scores indicating more severe neurologic impairment.
‖ In some cases, a relative or independent physician vouched for the patient before enrollment in the study, or an application for legal representation was used in lieu of informed consent before enrollment. Written informed consent was obtained from all patients or their legal representatives after enrollment.

Table 2. Secondary Outcomes at 12 Months.*

Outcome	Hemicraniectomy Group (N=49)	Control Group (N=63)	P Value	
			Intention-to-Treat Population	Surviving Patients
	no. of patients/total no. (%)			
Modified Rankin scale score			<0.001	0.73
0–2	0/47	0/62		
3	3/47 (6)	3/62 (5)		
4	15/47 (32)	7/62 (11)		
5	9/47 (19)	5/62 (8)		
6	20/47 (43)	47/62 (76)		
NIHSS total score			<0.001	0.70
17–42	7/22 (32)	3/10 (30)		
8–16	14/22 (64)	4/10 (40)		
0–7	1/22 (5)	3/10 (30)		
Barthel index score			0.002	0.34
60–100	3/27 (11)	5/13 (38)		
0–55	24/27 (89)	8/13 (62)		
SF-36 score†			<0.001	0.86
Mental component				
51–100	10/25 (40)	6/12 (50)		
26–50	14/25 (56)	6/12 (50)		
0–25	1/25 (4)	0/12		
Physical component			<0.001	0.43
26–100	11/25 (44)	5/12 (42)		
0–25	14/25 (56)	7/12 (58)		
Hamilton Depression Rating Scale score ‡			<0.001	0.97
0–19	18/18 (100)	5/6 (83)		
20–52	0/18	1/6 (17)		
EQ-5D visual-analogue scale score§			<0.001	0.94
51–100	6/22 (27)	2/10 (20)		
26–50	10/22 (45)	5/10 (50)		
0–25	6/22 (27)	3/10 (30)		

* There were 27 known survivors in the surgery group and 15 known survivors in the control group.
† Both the mental-component and physical-component summary scores of the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) range from 0 to 100, with higher scores indicating greater well-being. In this study, no patients had a mental-component summary score higher than 75 and no patients had a physical-component summary score higher than 50.
‡ Scores on the Hamilton Depression Rating Scale range from 0 to 52, with higher scores indicating greater severity of symptoms and scores higher than 19 indicating severe depression.
§ Scores on the EuroQoL Group 5-Dimension Self-Report Questionnaire (EQ-5D) visual-analogue scale range from 0 (worst quality of life) to 100 (best quality of life).

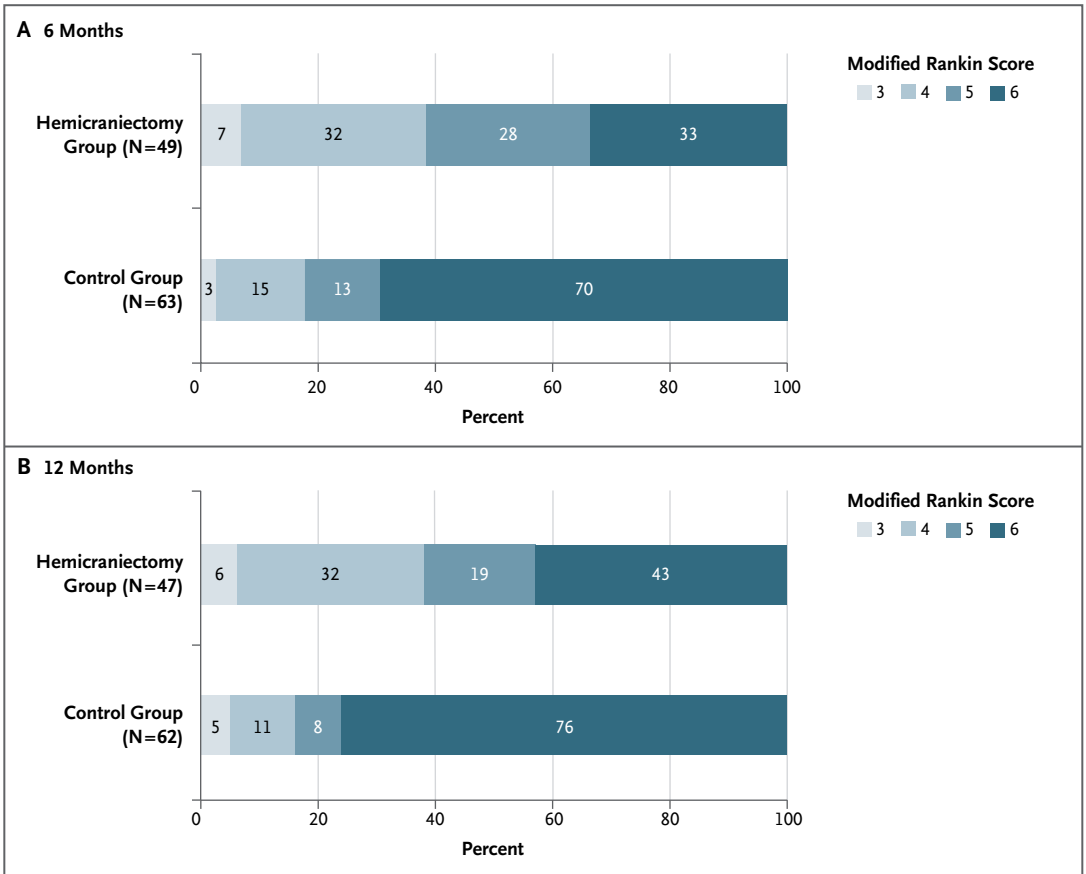

Figure 1. Functional Outcome after Hemicraniectomy and after Conservative Treatment Alone According to the Modified Rankin Score.

The primary end point was survival without severe disability, defined as a score of 0 to 4 on the modified Rankin scale (range, 0 to 6, with 0 indicating no symptoms and 6 indicating death). The results shown are the probability estimates for all patients who underwent randomization (the intention-to-treat population). Panel A shows the bias-corrected distribution of scores on the modified Rankin scale at 6 months. Panel B shows the raw distribution of Rankin scores at 12 months.

(Table S6 in the Supplementary Appendix). Infections were more frequent in the hemicraniectomy group. In addition, 23 complications related to initial hemicraniectomy and bone-flap reimplantation were reported: 5 hemorrhages, 10 cases of pain requiring pharmacologic treatment, 1 hygroma, 1 incident related to anesthesia, and 6 nonspecified events, 5 of which were classified as serious adverse events. The most frequent serious adverse events in the control group were nervous system disorders (mainly herniation and brain edema). Causes of death are listed in Table 3. An increased rate of early death due to herniation in the control group was the only major difference between the two treatment groups.

DISCUSSION

The DESTINY II trial was stopped for reasons of efficacy after the reductions in deaths and severe disability at 6 months had become significant. This treatment effect remained stable after inclusion of all randomly assigned patients and after 12 months of follow-up.

The question of an age limit for hemicraniectomy in patients with malignant middle-cerebral-artery infarction is controversial among neurologists and neurosurgeons. The uncertainty about whether surgery is beneficial in older patients with stroke, for whom the overall prognosis is poorer than that for younger patients with stroke,

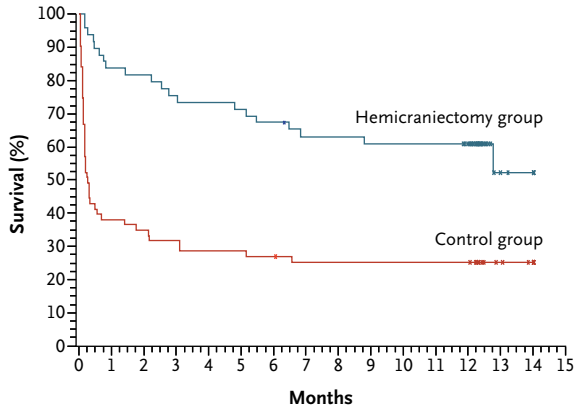

Figure 2. Kaplan–Meier Estimates of Survival in the Hemicraniectomy and Control Groups.

The effect of hemicraniectomy in reducing mortality was clearly due to increased survival rates in the early phase, but it remained stable throughout the whole observation period.

stems from heterogeneous results of retrospective and uncontrolled observational studies and is reflected in numerous reviews and commentaries.[11-13,21-28]

Our randomized trial provides comparative evidence regarding the efficacy of hemicraniectomy in patients older than 60 years with malignant middle-cerebral-artery infarction. The benefit of hemicraniectomy with respect to the primary end point was significant. However, the size of the difference between the groups was smaller than that observed in similar trials involving younger patients and was mainly driven by the reduction in mortality. After 12 months, only 6% of the patients older than 60 years of age who underwent hemicraniectomy had a score of 3 on the modified Rankin scale, whereas 43% of younger patients had a score of 3 or even 2. This result was not unexpected.[14] In general, the outcome after stroke is age-dependent, and chances for a better outcome decrease with age. In this trial, surgery reduced 1-year mortality by 33%, as compared with a 50% reduction in a prior trial involving younger patients, and the rate of survival with a score of 5 on the modified Rankin scale at 1 year was 19%, as compared with 4% among younger patients.[5]

The score on the modified Rankin scale is frequently dichotomized as a "favorable" or "unfavorable" outcome to estimate the benefit of a therapy. For patients who survive malignant middle-cerebral-artery infarcts, these terms are probably not adequate, and they sparked controversial discussions after the randomized hemicraniectomy trials involving younger patients.[29,30] The terms "acceptable" and "unacceptable" may be more appropriate for a disease with a proven treatment that is lifesaving but results in survival with moderate or severe disability, but this is a discussion that goes beyond the report of this trial. Survival with substantial disability instead of death is an outcome that may be acceptable to some patients and caregivers and may not be acceptable to others. A majority of patients and caregivers gave retrospective consent to the treatment they received. This result should be interpreted with caution, given that 25 of 42 survivors (16 in the hemicraniectomy group and 9 in the control group) could not adequately answer this question because of severe aphasia or neuropsychological deficits. Nonetheless, this finding is consistent with observations in younger patients.[31]

Standard outcome measures such as the modified Rankin scale, the Barthel index, and the NIHSS focus on motor abilities but neglect other relevant deficits. Disability, however, is a complex construct that includes factors such as status with respect to depression, coping strategies, and cognitive functions, which are not assessed by these scales. In DESTINY II, we included a number of established instruments to evaluate other dimensions of the outcome after severe stroke. Quality of life assessed by means of the EQ-5D and the SF-36 was clearly impaired in survivors in our trial as compared with patients with less severe stroke and persons 60 years of age or older in the general population (Fig. S8 in the Supplementary Appendix).[19,20] It was, however, similar to that of survivors of severe traumatic brain injury, subarachnoid hemorrhage, or intracerebral hemorrhage.[32-35] Quality of life was also similar to or even better than that in younger patients with malignant middle-cerebral-artery infarcts.[8]

Symptoms of depression are common in stroke survivors. Among survivors in our trial who were able to complete the depression scale, the frequency of major depression was similar to the

Table 3. Causes of Death.

Variable	Hemicraniectomy Group (N=49)	Control Group (N=63)
Total deaths — no.	20	47
Deaths from 0–14 days after randomization — no. of deaths/total no. (%)		
Neurologic: herniation	4/20 (20)	34/47 (72)
Non-neurologic: pneumonia, myocardial infarction, or sepsis	1/20 (5)	2/47 (4)
Total	5/20 (25)	36/47 (77)
Deaths from 15 days–12 mo after randomization — no. of deaths/total no. (%)		
Neurologic: new contralateral infarct	2/20 (10)	2/47 (4)
Non-neurologic		
Pulmonary embolism	2/20 (10)	0/47
Pneumonia, sepsis	5/20 (25)	4/47 (9)
Myocardial infarction	0/20	2/47 (4)
Unknown	6/20 (30)	3/47 (6)
Total	15/20 (75)	11/47 (23)

reported frequencies in the overall population of patients with stroke, among patients with cerebral hemorrhage, and among younger patients with malignant middle-cerebral-artery infarcts.[8,31,36-39] These results should be interpreted cautiously, because depression was assessed in only 57% of survivors because of aphasia.

The number of serious adverse events was similar in the two treatment groups. The slight excess in numbers in the hemicraniectomy group is best explained by the longer survival time and the longer stay in the ICU, reflected in the numerically higher rate of infections in the surgery group. In the control group, the excess of serious adverse events related to the central nervous system was due to herniation, which was the leading cause of death in the trial.

Despite our observation of the efficacy of hemicraniectomy in older patients with malignant middle-cerebral-artery infarction, the treatment decision for such patients remains difficult. One may argue that survival with a score worse than 3 on the modified Rankin scale is not an acceptable outcome. Certainly, the quality of life and activities of daily living were considerably impaired in our patients who underwent hemicraniectomy, but these outcomes are similar to those in patients who have sustained other severe brain injuries. Our trial provides helpful information for health professionals, patients, and their caregivers who must decide whether or not to pursue hemicraniectomy. This trial showed that the most probable alternative to early hemicraniectomy is death. Most patients who underwent hemicraniectomy and survived had subsequent disability that was moderate or severe. Only a small minority of older patients who underwent hemicraniectomy survived without disability severe enough to require assistance with most bodily needs, and one third of the survivors had very severe disability (complete dependence according to the Barthel index).

In conclusion, early hemicraniectomy significantly increased the probability of survival among patients older than 60 years of age with malignant middle-cerebral-artery infarction, but most survivors had substantial disability. Important questions such as the long-term effect of chronic disability and patient characteristics associated with a greater or lesser benefit from hemicraniectomy require further research.

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Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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