Hemicraniectomy versus Conservative Treatment in Large Hemispheric Ischemic Stroke Patients: A Meta-analysis of Randomized Controlled Trials

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Background: Several small trials have inconclusively evaluated the effect of hemicraniectomy in reducing death and disability in acute ischemic stroke patients with large hemispheric infarctions. We compared the effects of hemicraniectomy on death and disability with conservative treatment in patients with large hemispheric infarctions. *Methods:* We calculated pooled odds ratios (ORs) and 95% confidence intervals (CIs) using random-effects models from 7 randomized trials that compared hemicraniectomy with conservative treatment in acute ischemic stroke patients. The primary end point was a favorable outcome defined by modified Rankin Scale grades of 0 (no symptoms), 1 (no significant disability), 2 (slight disability), and 3 (moderate disability) at 6-12 months post randomization. *Results:* Of the 341 total subjects randomized, the proportion of subjects who achieved a favorable outcome was significantly greater among those randomized to hemicraniectomy than among those randomized to conservative treatment (OR 2.04, 95% CI 1.03-4.03, $P = .04$). Survival was also significantly greater among those randomized to hemicraniectomy (OR 5.56, 95% CI 3.40-9.08, $P < .001$) than among those randomized to conservative treatment. There was a trend toward higher odds of favorable outcome among those randomized to hemicraniectomy than among those randomized to conservative treatment in trials that permitted recruitment of patients aged 60 years or older (303 subjects analyzed; OR 1.87, 95% CI .91-3.86, $P = .09$). *Conclusions:* Compared with conservative treatment, the odds of achieving a favorable outcome at 6 months is approximately 2-folds higher with hemicraniectomy in patients with large hemispheric infarctions. **Key Words:** Hemicraniectomy—meta-analysis—mortality—disability—acute ischemic stroke—surgical decompression.

Decompressive hemicraniectomy is a procedure for patients with malignant middle cerebral artery territory infarction to reduce mass effect and intracranial hypertension, and subsequently to reduce death and disability.[1] The value of the procedure and appropriate indications are debated because of concerns regarding reducing mortality but increasing severe disability among those who undergo the procedure.[2-4] The utilization of the procedure has increased in United States over the years[5]; however, no major change has been observed in response to publication of randomized clinical trials that demonstrate superiority of hemicraniectomy over conservative management in patients with ischemic stroke.[6] Although several trials have been completed, the small number of subjects recruited prevents conclusive assessment of the magnitude of benefits associated with

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hemicraniectomy in ischemic stroke patients. A meta-analysis of 3 randomized clinical trials was performed and reported in 2007.[7] Subsequently, 2 meta-analyses provided conflicting results regarding the effect of hemicraniectomy on the reduction of disability.[8,9] We performed this meta-analysis to incorporate the results of recent clinical trials[10-16] that have been reported since the previous meta-analysis and to provide a more rigorous assessment of the therapeutic benefit of the procedure.

Methods

Study Design

We performed a meta-analysis of relevant randomized controlled trials. We followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses guidelines for systematic reviews and meta-analyses (see Fig 1). We performed a computerized literature search of the MEDLINE and Cochrane databases on December 28, 2015, with the following search terms: "clinical trials," "craniectomy," "middle cerebral artery," "decompressive surgery," "malignant artery infarction," "randomized trials," "stroke," "cerebral edema," "hemicraniectomy," "standardized medical management," and "acute ischemic stroke." No other search restrictions were applied.

We included trials if they enrolled patients with acute ischemic stroke and randomly assigned patients to hemicraniectomy or conservative treatment within 7 days of symptom onset. Trials that included less than 10 subjects, those that did not report clinical outcomes according to grades of modified Rankin Scale at 6-12 months post randomization, or those that performed procedures for post-thrombolytic intracranial hemorrhage were excluded.

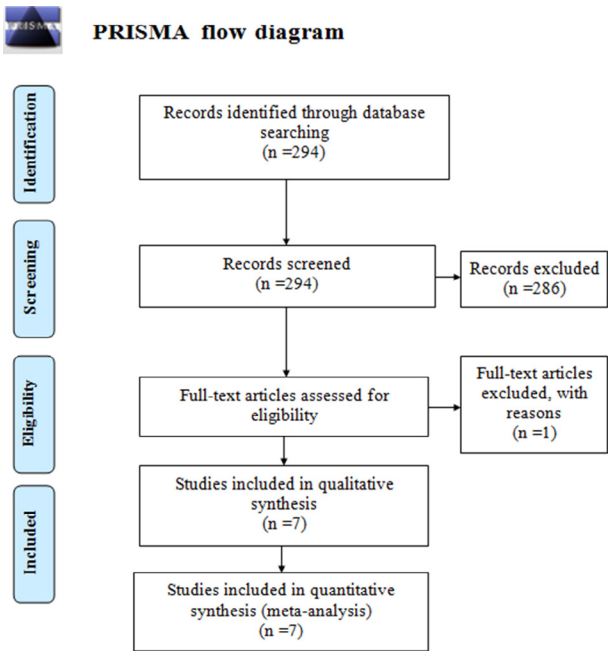

Figure 1. *Identification of studies included in the meta-analysis. Abbreviation: PRISMA, Preferred Reporting Items for Systematic reviews and Meta-Analyses.*

Outcomes

The primary efficacy end point was the proportion of randomized subjects who achieved favorable outcome defined by modified Rankin Scale grades of 0 (no symptoms), 1 (no significant disability), 2 (slight disability), or 3 (moderate disability) at 6-12 months post randomization. Five trials[10,11,13,15,16] reported outcomes at 6 months and 2 trials[12,14] reported outcomes at 12 months post randomization. Secondary efficacy end points were the proportion of randomized subjects who achieved modified Rankin Scale grades of 0-4 and also survival at 6-12 months post randomization. Information on these end points was abstracted by 2 investigators independently and was entered into a structured dataset and compared. All disagreements were resolved by reaching consensus and there was complete agreement on abstracted results in the final dataset.

Statistical Analysis

The odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using Comprehensive Meta-Analysis 2.2.048; (Biostat Inc., Englewood, NJ) for each of the trial. We compared the calculated ORs with the ORs or hazard ratios reported in the original manuscript when available to ensure congruence. We attempted to include every trial, and trials in which specific end points were not reported were excluded only from the pooled analyses of the specific end points that were not reported.

The pooled odd ratios were estimated using a random-effects model using the method described by DerSimonian and Laird.[17] We assessed heterogeneity and the magnitude of heterogeneity for each specific end point using the Cochran Q statistic and the I^2 measure (the percentage of total variability due to true between-study heterogeneity), respectively. We analyzed data in strata defined by whether the trial permitted recruitment of patients aged 60 years or older and if patients were randomized within 72 hours of diagnosis of middle cerebral artery infarction. We assessed publication bias by using Egger's intercept P value (2-sided) and by visual inspection of funnel plots. For sensitivity analysis, the effect of sizes of all included trials was combined using a fixed-effects model.[18] All tests were 2-sided, with P less than .05 deemed significant.[19]

Results

We identified 8 randomized clinical trials evaluating heimcraniectomy in acute ischemic stroke patients.[10-16,20] One trial[20] was excluded because it used Glasgow Coma Scale as outcome measure. Theremaining 7 trials met the