



Hemispherectomy: The Full Half of the Glass

Longitudinal Seizure Outcome and Prognostic Predictors After Hemispherectomy in 170 Children.

Moosa AN, Gupta A, Jehi L, Marashly A, Cosmo G, Lachhwani D, Wyllie E, Kotagal P, Bingaman W. *Neurology* 2013;80:253–260.

OBJECTIVE: Data on longitudinal seizure outcome after hemispherectomy in children are limited. This study explores the posthemispherectomy longitudinal seizure outcome and its predictors. **METHODS:** We reviewed 186 consecutive children who underwent hemispherectomy between 1997 and 2009 at our center. Clinical, EEG, imaging, and surgical data were collected. Seizure outcome data were collected via a structured questionnaire by contacting families (n = 125) or from the medical records at last follow-up (n = 58). **RESULTS:** Of 186 patients, 3 were lost to follow-up; 13 seizure-free patients with new-onset nonepileptic spells were excluded. Perioperative complications were not collected. There was no mortality. At a mean follow-up of 5.3 years (± 3.3 years), 112 of 170 children (66%) were seizure-free (Engel class 1a). In 58 patients with seizure recurrence, 8 had late remission and 16 had >90% reduction. Overall, at last follow-up, 136 patients (80%) were either seizure-free or had major improvement. Using survival analysis, the estimated probability of seizure freedom after hemispherectomy was 78% (95% confidence interval [CI] = 75%–81%) at 6 months, 76% (95% CI = 73%–79%) at 1 year, 71% (95% CI = 68%–74%) at 2 years, and 63% (95% CI = 59%–67%) at 5 years. On multivariate analysis, bilateral PET abnormalities (risk ratio = 2.53, 95% CI = 1.02–5.85) and acute postoperative seizures (risk ratio = 7.03, 95% CI = 3.07–15.9) independently predicted seizure recurrence. **CONCLUSIONS:** The long-term seizure-free rates after hemispherectomy remained stable at 63% at 5 years and beyond. This study will assist in better candidate selection for hemispherectomy, presurgical counseling, and early identification of surgical failures.

Commentary

Hemispherectomy was introduced by Walter Dandy in 1928 for removal of a right hemispheric glioma (1) but was pioneered for use in catastrophic epilepsy by McKenzie a decade later (2). The procedure was abandoned for years due to its morbidity and mortality but was repopularized in 1950 by Krynauw, who used it to treat infantile hemiplegia (3). The techniques of hemispherectomy then underwent many changes over the years, with Rasmussen developing the notion of functional hemispherectomy in 1974, which in turn, underwent further modifications with very low mortality rates (4). Hemispherectomy is now a well-established procedure for holohemispheric drug-resistant epilepsies, constituting 20–40% of all pediatric epilepsy surgeries at some centers (5). These epilepsies are often associated with hemimegalencephaly, porencephaly, malformations of cortical development, Sturge–Weber syndrome, infantile hemiplegia, and Rasmussen's encephalitis. Other etiologies that may be appropriate for hemispherectomy include stroke, trauma, arteriovenous malformations, hemiatrophy, and tuberous sclerosis. Candidates for hemispherectomy typically have hemiparesis and other baseline neurologic deficits that lateralize to the epileptic hemisphere.

Furthermore, due to its overall long-term cognitive, behavioral, and psychosocial benefits, this surgery is also recommended in individuals who have retained some functions in the diseased hemisphere, especially when surgery is performed early. Such improvements often outweigh any worsening of motor impairments (6). Additionally, the young brain has remarkable plasticity that facilitates reorganization of eloquent functions. This is exemplified by a child whose baseline language fMRI lateralized to the left, but after left hemispherectomy, the fMRI showed evidence of later reorganization of language functions to the right (7).

Moosa et al. studied 186 children who underwent hemispherectomy by a single surgeon (8), with the goal of assessing longitudinal outcome of seizure freedom rates by survival analysis, and predictors of seizure outcome by proportional hazard modeling. They excluded 3 patients due to loss of follow-up and 13 due to emergence of non-epileptic paroxysmal events. Of the remaining 170 patients, 112 (66%) were seizure free after a mean follow-up period of 5.3 (± 3.3) years. Of those who experienced seizure recurrence, 8 patients achieved late remission and 16 achieved more than 90% reduction of seizure frequency, increasing the number of patients achieving major improvement to 136 patients (80%). In addition, the authors mention that the 13 excluded subjects with nonepileptic events also experienced resolution of their habitual seizures. Interestingly, 76 (67%) of the seizure-free subjects were not on antiepileptic medications. Survival analysis found a seizure



freedom rate of 86% at 3 months, dropping to 63% at 5 years or beyond.

Univariate analysis found that acute postoperative seizures (defined as seizures occurring within one week of the surgery), non-lateralizing ictal EEG, and bilateral PET abnormalities predicted seizure recurrence. Of these, bilateral PET abnormalities and acute postoperative seizures independently predicted seizure recurrence on multivariate Cox proportional hazard analysis, with the risk of seizure recurrence being 7 times higher in patients with acute postoperative seizures. Moreover, 54% of all patients who failed hemispherectomy experienced their seizure recurrence within 4 postoperative months. Of importance, there were no differences between seizure-free and seizure-recurrence groups with regards to preoperative seizure frequency, localization of preoperative interictal epileptiform discharges, etiology, baseline motor deficits, or brain MRI findings in the contralateral hemisphere. The authors concluded that metabolic abnormalities in the contralateral hemisphere on PET may be more predictive of seizure outcome than contralateral MRI abnormalities. Some of the subjects in this cohort had undergone previous surgery, and hemispherectomy resulted in seizure freedom in 35% of patients who had failed previous hemispherectomy and in 78% of those who had failed focal resection.

The outcome reported in this study is in line with previous results. Across studies, seizure reduction rates after hemispherectomy have ranged between 50% and 92%, with very low mortality rates (4). However, this study's peculiar strengths lie in its large sample size of 170 subjects and in the duration of follow-up: Almost half the subjects in this cohort had a follow-up of at least 5 years, with more than one-fifth followed up for at least 8 years. This facilitated conduction of a survival analysis that can be very helpful when counseling patients and their families about chances of continued seizure freedom as a function of time. The large cohort also facilitated answering chronic questions about the significance of various risk factors for seizure recurrence. For example, previous studies often correlated the outcome with etiology (4); this was not supported by the study discussed here.

Although this is a single-center experience, the concordance of the conclusions with data from other centers confirms the great utility of hemispherectomy in intractable holohemispheric epilepsy. For example, other authors have similarly found that acute postoperative seizures (also defined as seizures in the first postoperative week) are associated with seizure recurrence (9, 10) and that such seizures should encourage early evaluation of surgical failure. In addition, the current results confirm known findings that bilateral ictal EEG does not exclude patients from hemispherectomy (11) and, even more importantly, that contralateral

MRI findings do not contraindicate surgery (5). Future studies should focus more on motor and cognitive outcomes after hemispherectomy in light of the duration of epilepsy, age at surgery, presurgical functioning, and etiology, in addition to postoperative seizure outcome. A better understanding of outcome predictors will help plan more adequate postsurgical rehabilitation. Finally, a recent nationwide pediatric inpatient database analysis concluded that the annual performance of hemispherectomy is still infrequent, likely due to the few tertiary high-volume centers that can perform the procedure (4). Perhaps the positive outcomes reported in this study will encourage increased consideration of hemispherectomy in epilepsy centers.

by Mohamad Koubeissi, MD

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