

EPILEPSY SURGERY IN THE FRONTAL LOBE: *TERRA INCOGNITA* OR NEW FRONTIER?

Surgical Outcome and Prognostic Factors of Frontal Lobe Epilepsy Surgery. Jeha LE, Najm I, Bingaman W, Dinner D, Widdess-Walsh P, Luders H. *Brain* 2007;130(Pt 2):574–584. Epub 2007 Jan 5. Frontal lobe epilepsy (FLE) surgery is the second most common surgery performed to treat pharmacoresistant epilepsy. Yet, little is known about long-term seizure outcome following frontal lobectomy. The aim of this study is to investigate the trends in longitudinal outcome and identify potential prognostic indicators in a cohort of FLE patients investigated using modern diagnostic techniques. We reviewed 70 patients who underwent a frontal lobectomy between 1995 and 2003 (mean follow-up 4.1 ± 3 years). Data were analysed using survival analysis and multivariate regression with Cox proportional hazard models. A favourable outcome was defined as complete seizure-freedom, allowing for auras and seizures restricted to the first post-operative week. The estimated probability of complete seizure-freedom was 55.7% [95% confidence interval (CI) = 50–62] at 1 post-operative year, 45.1% (95% CI = 39–51) at 3 years, and 30.1% (95% CI = 21–39) at 5 years. Eighty per cent of seizure recurrences occurred within the first 6 post-operative months. Late remissions and relapses occurred, but were rare. After multivariate analysis, the following variables retained their significance as independent predictors of seizure recurrence: MRI-negative malformation of cortical development as disease aetiology [risk ratio (RR) = 2.22, 95% CI = 1.40–3.47], any extrafrontal MRI abnormality (RR = 1.75, 95% CI = 1.12–2.69), generalized/non-localized ictal EEG patterns (RR = 1.83, 95% CI = 1.15–2.87), occurrence of acute post-operative seizures (RR = 2.17, 95% CI = 1.50–3.14) and incomplete surgical resection (RR = 2.56, 95% CI = 1.66–4.05) (log likelihood-ratio test P -value < 0.0001). More than half of patients in favourable prognostic categories were seizure-free at 3 years, and up to 40% were seizure-free at 5 years, compared to <15% in those with unfavourable outcome predictors. These data underscore the importance of appropriate selection of potential surgical candidates.

COMMENTARY

The temporal lobectomy has been the most common neurosurgical treatment for medically intractable focal epilepsy. Its effectiveness has been well demonstrated, most

recently by a randomized controlled trial (1). Nonetheless, a substantial portion of intractable epilepsy originates outside the mesial temporal region, and as epilepsy surgery has become more widely available, large academic epilepsy centers are evaluating greater numbers of extratemporal epilepsy patients for neurosurgical treatment. The overall chance of seizure freedom from resections in extratemporal regions is acknowledged to be lower than that of temporal resections, however, past literature shows quite variable outcomes and prognostic indicators for

frontal lobe epilepsy surgery (2–4). When should neurosurgical treatment be considered for frontal lobe epilepsy?

In this regard, the report by Jeha et al. is welcome because it presents a carefully analyzed series of 70 frontal epilepsy resections over a 9-year period, excluding only patients with prior neurosurgery, resections extending outside the frontal lobe, or with less than 1 year of follow-up. This series represents outcomes of patients for whom the best diagnostic and surgical techniques available were used, representing a “snapshot” of the best therapeutic approaches of the recent past. It demonstrates a rate of seizure-freedom that justifies neurosurgical treatment for many subgroups of frontal epilepsy patients.

The most significant finding of the study concerns the strong effect of particular factors on patient outcome. The preoperative clinical characteristics of patients, such as gender, age at the time of seizure onset or operation, family history, and seizure types and frequency, did not significantly affect prognosis. Multivariate analysis demonstrated that a seizure-free outcome depended on accurately locating the seizure focus, defining its full extent, and removing all of it, since the significant predictive factors were MRI findings, interictal and ictal EEG findings, and completeness of resection. After surgery, occurrence of auras or immediate postoperative seizures was a negative predictor. In the subset of patients with favorable prognostic factors on multivariate analysis, seizure-free outcome approached that seen for temporal lobectomy, with a 50% to 60% seizure-free rate at 3 years, while the rate was only 0% to 14% for those with unfavorable factors. There were 12 patients who had all favorable prognostic factors, with localized and completely resected MRI lesions, localizing ictal EEG, and no acute postoperative seizures; 11 of these 12 were completely seizure free at the last follow-up.

A strength of this report is the longitudinal analysis, since surgical outcome is very much a function of duration of follow-up. The analysis reveals a significant decrease in complete seizure freedom over the 5-year period following surgery—much like what has been described after temporal lobectomy (5–7). However, recurrence tended to happen earlier in this frontal lobe series, with 80% occurring in the first 6 months. Of concern, recurrence also was more persistent, with 60% of the failing patients not seizure-free at the last follow-up. However, seizure-freedom at 3 and 5 years was significantly higher in patients with favorable prognostic factors.

Univariate analysis of the effect of etiology on patient outcome was informative. Twenty-one patients had a well-defined etiology of neoplasm, vascular malformation, or encephalomalacia, with 12 individuals achieving seizure freedom. Seven were cryptogenic, with normal MRI and pathology, and only two of

these seven became seizure free. The largest group was made up of 41 patients with cortical developmental malformations. It is this group that poses the greatest challenge for presurgical diagnostic evaluation. Fifteen of 29 patients with MRI-positive malformations were completely seizure-free. In contrast, 11 of 12 with MRI-negative, but pathologically demonstrated cortical developmental malformations had seizure recurrence. This finding implies that correct localization of a seizure focus, as documented by neuropathology, is not sufficient to produce a good outcome if the full extent of the pathology cannot be outlined for complete surgical removal. When fully characterized by neuroimaging, cortical dysplasia, and other developmental malformations are amenable to successful surgical treatment.

This study confirms that treatment of medically intractable cases with well-delineated and totally removable seizure foci in the frontal lobe is familiar territory and that these patients most definitely are surgical candidates. In contrast, the evaluation of those with poorly defined dysplasia or normal MRI represents *terra nova*—a new frontier, in which diagnostic innovations are needed to improve outcomes and extend the benefits of frontal lobe epilepsy surgery to more individuals.

by John W. Miller, MD, PhD

References

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