

MORE LONG-TERM OUTCOME DATA ON TEMPORAL LOBECTOMY

Temporal Lobectomy: Long-term Seizure Outcome, Late Recurrence, and Risks for Seizure Recurrence

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Little information is available relevant to long-term seizure outcome after anterior temporal lobectomy, particularly at extended postoperative periods. The aim of this study was an in-depth examination of patterns of longitudinal outcome and potential risk factors for seizure recurrence after lobectomy, using a large patient sample with long follow-up. Included were 325 patients who underwent anterior temporal lobectomy between 1978 and 1998 (mean follow-up, 9.6 ± 4.2 years). Retrospective data were analyzed by using survival analysis and multivariate regression with Cox proportional hazard models. The probability of complete seizure freedom at 2 years after surgery was 55.3% (95% confidence interval [CI], 50 to 61); at 5 years, 47.7% (95% CI, 42 to 53); and at 10 postoperative years, it was 41% (95% CI, 36 to 48). Patients with discrete preoperative abnormalities (i.e., lesions and hippocampal sclerosis) had a significantly higher probability of seizure freedom than did patients without obvious abnormality. The latter group had a pattern of recurrence similar to that in patients with lesions outside the area of excision. After adjustment for preoperative pathology, only the presence of preoperative secondarily generalized seizures had a significant

association with recurrence (occasional preoperative generalized seizures: hazard ratio [HR], 1.6; 95% CI, 1.1 to 2.3; frequent seizures: HR, 2.0; 95% CI, 1.4 to 2.9, compared with absence of preoperative generalized seizures). Duration of preoperative epilepsy, age at seizure onset, and age at surgery did not have an effect on outcome. Patients with two seizure-free postoperative years had a 74% (95% CI, 66 to 81) probability of seizure freedom by 10 postoperative years. This late seizure recurrence was not associated with any identified risk factors. Specifically, patients with hippocampal sclerosis were not at higher risk. Surprisingly, complete discontinuation of antiepileptic drugs (AEDs) after 2 postoperative years was not associated with an increased risk of recurrence (HR, 1.03; 95% CI, 0.5 to 2.1). This may be because selection of patients for AED discontinuation is biased toward those individuals perceived as “low risk.” The results of this study indicate that the lack of an obvious abnormality or the presence of diffuse pathology, and preoperative secondarily generalized seizures are risk factors for recurrence after surgery. Late recurrence after initial seizure freedom is not a rare event; risk factors specific to this phenomenon are as yet unidentified.

COMMENTARY

Historically, views on the surgical treatment of pharmacoresistant epilepsy largely have been informed by a variety of reports describing the short-term response to surgical intervention, as well as by accumulated clinical experience. More recently, several retrospective long-term studies (1,2) and, finally, well-designed, prospective clinical trials (3,4) have provided even more robust outcome data. Results after surgical treatment of temporal lobe epilepsy have dominated the literature, certainly, because that syndrome is relatively common and is among the most surgically responsive conditions.

The present report by McIntosh and colleagues is yet another retrospective analysis of clinical outcomes after the surgical treatment of medically refractory temporal lobe epilepsy. What sets it apart from other studies, and the reason it deserves highlighting, is its distinctive features. The analysis pertains to an especially large cohort of patients ($N = 325$), for whom

truly long-term follow-up (a mean of 10 years) information was available—with very few patients (3%) lost to follow-up. Furthermore, contemporary approaches were used to characterize the underlying pathology in each patient, making these retrospective cases far more relevant to modern interpretation. In addition, rigorous statistical methods bring added certainty to the conclusions drawn by the authors.

This study analyzed 325 patients, in a single Australian epilepsy program, who underwent temporal lobe resection over a 20-year period (1978–1998). Characterization of each patient's underlying pathology (e.g., hippocampal sclerosis, foreign-tissue lesions, other temporal lobe lesions [such as dysplasia or posttraumatic gliosis], distant lesions outside the area of surgical excision) or determination of the lack of obvious pathology was accomplished by using modern interpretation of surgical pathology specimens and/or magnetic resonance imaging (MRI) findings by blinded raters. Kaplan–Meier analysis

was used to calculate the probability of postoperative seizure freedom and of late (i.e., ≥ 2 postoperative years) seizure recurrence. The influence of a variety of factors (e.g., pathology, age at onset of epilepsy, duration of epilepsy, age at surgery, presence of secondarily generalized seizures, and discontinuation of antiepileptic drugs [AEDs]) on outcome was assessed by using multivariate statistical techniques.

Seizure-free outcomes (defined as no seizures, only persistent auras, or seizures limited to the immediate postoperative period), for the group as a whole, occurred in 61% of patients at 1 year, 55% at 2 years, 48% at 5 years, and 41% at 10 years. The authors point out a sobering finding from their analysis: even for those patients who have achieved seizure freedom at the 2-year postoperative time point, one fourth of these individuals will have experienced seizure recurrence by the 10-year mark. The probability of remaining free from seizures on the tenth postoperative anniversary was highest in those patients whose underlying pathology consisted of a foreign-tissue lesion or hippocampal sclerosis, about 63% and 50%, respectively. In contrast, patients with normal pathology or those classified as having other types of pathology confined to the temporal lobe (such as dysplasia) had a poor long-term prognosis, with only about 13% and 19% seizure free at 10 years. Of the other factors previously mentioned, only the presence of preoperative secondarily generalized seizures had a significant association with postoperative seizure recurrence. Postoperative discontinuation of AEDs, however, was not associated with a greater likelihood for seizures to recur.

Pitfalls exist in retrospective studies—especially one that traverses treatment protocols over a 2-decade period, during which seizure-localization and operative techniques were rapidly evolving. This careful study attempted to mitigate one of the potential problems in using historical data, namely, the inaccurate characterization of the underlying epileptogenic pathology. The authors retrieved the surgical specimens for updated analysis and coupled this with modern interpretation of MRI studies, in an attempt to arrive at the most accurate final diagnosis of pathology for each patient.

Do any surprises result from this long-term analysis? One unanticipated finding might be the somewhat disappointing 50% rate of seizure freedom in the hippocampal sclerosis group at 10 years. Modern experience certainly suggests a much higher shorter-term success rate. Of course, resective surgery currently

constitutes the most effective treatment for pharmacoresistant medial temporal lobe epilepsy associated with hippocampal sclerosis, but based on the report of McIntosh and colleagues, restrained optimism for long-term retention of seizure control seems to be in order. Another unexpected finding might be the lack of association between AED discontinuation and seizure recurrence. Nevertheless, the authors do point out that this observation might reflect the greater likelihood of drug discontinuation being undertaken in those patients perceived by clinicians to have the lowest risk of seizure recurrence, because medication discontinuation was not approached on a systematic basis across the cohort of patients.

Retrospective series that include cases dating back to the pre-MRI era undoubtedly cannot fully replicate contemporary practice in which advanced imaging and neurophysiology techniques, as well as intraoperative surgical navigation technology, are available. The impact of this evolution in diagnostic and therapeutic capability probably is most pertinent to outcomes for those patients who have less discrete pathology, such as cortical dysplasia. Indeed, in the present series, it was just those patients who had the poorest outcome. Yet, thoughtful retrospective analyses of patients treated with epilepsy surgery—such as the one highlighted here—and prospective studies in the modern era are gradually bringing the full landscape of postsurgical outcomes into view.

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