

EPILEPSY SURGERY: ARE YOU EVER OUT OF THE WOODS?

Long-Term Seizure Outcome In Patients Initially Seizure-Free after Resective Epilepsy Surgery

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PURPOSE: To evaluate the likelihood of and risk factors for seizure recurrence in patients initially seizure free after resective surgery for intractable epilepsy.

METHODS: One hundred seventy-five patients who underwent lobectomy between 1972 and 1992 and were seizure free during the first postoperative year were retrospectively studied. Outcome was measured by relapse risk, presence of auras in otherwise seizure-free patients, and seizure frequency among relapsers. Factors significant in bivariate or Kaplan–Meier analysis or considered potentially predictive *a priori* were included in multivariate models.

RESULTS: Of the 175 patients (mean follow-up, 8.4 years), 63% never relapsed. The likelihood of being seizure free was $83\% \pm 6\%$ 3 years after surgery, $72\% \pm 7\%$ after 5 years, and $56\% \pm 9\%$ after 10 years. After adjusting for age at surgery, duration of preoperative epilepsy, and resection site, normal pathology was associated with increased risk of relapse compared with mesial temporal sclerosis or other pathology [$P = 0.036$; hazard ratio (HR) 2.38; 95% confidence interval (CI), 1.06–5.34]. Among patients otherwise seizure free, preoperative illness of ≥ 20 years was associated with increased risk of postoperative auras ($P = 0.040$; HR, 3.55; 95% CI, 1.06–11.90). Among relapsers, 51% experienced one or fewer seizures per year. Normal pathology and earlier relapse were associated with higher postoperative seizure frequency.

CONCLUSIONS: In patients seizure free during the first year after resective epilepsy surgery, the likelihood of remaining seizure free declined to 56% over a 10-year period, but half of patients who relapsed had at most one seizure per year. Longer preoperative illness and normal pathology predicted poorer outcome.

COMMENTARY

The retrospective study by Yoon and colleagues explores long-term, seizure-free outcome after epilepsy surgery. The population evaluated in detail was those patients who were seizure free for the first year after surgery. This group comprised 175 patients of the 371 who received surgery at the center from 1972 to 1992 (with callosotomy and hemispherectomy excluded). This study was carried out at one of the few centers in the United States that performed a large number of surgeries in the 1970s, thus providing a large sample and long follow-up. The majority of surgeries (80%) were temporal lobectomy. Surprisingly, no difference was found in long-term remission for temporal versus extratemporal resection in the study of Yoon et al. This result may be explained by the small number of extratemporal patients in this sample (35). We are not told how many of the original cohort of 371 were extratemporal resections, but presumably a larger percentage of extratemporal patients did not remain seizure free for even the first year.

The increased likelihood of seizure recurrence in patients with normal pathology compared with those with mesial temporal sclerosis, tumor, or other known cause is not too surprising. The fact that pathology was “normal” is another way of saying that etiology of seizures was unexplained, which could equate to missed cortical dysplasia or other more widespread pathology.

One concern about the study is the duration of follow-up. Follow-up ranged from 3 to 20 years, with a median of 8 years. About as many relapses occurred after 5 years as before, so it is likely that a few of the patients with shorter follow-up would relapse if followed up longer. It is not stated how many patients were unavailable for follow-up. The authors claim that if no follow-up was available in the medical record within the last year, “an attempt was made to locate and interview the patients by telephone.” However, they do not indicate whether they were successful. Therefore the relapse rate indicated in the article probably is conservative.

Fifty-five percent of relapses were “moderate” (>1 seizure/year, 49%) or “severe” (>1 seizure/month, 6%). Although this frequency of seizure is undoubtedly lower than the presurgery seizure rate, it is enough to prevent driving and to affect social functioning. A patient who has been enjoying a seizure-free existence for 3, 4, or 5 years may have significant

difficulty with returning to a life that includes dealing with even rare seizures.

An editorial accompanying the article by Yoon et al. compares the outcome of epilepsy surgery with the outcome of refractory patients in general and urges early referral for epilepsy surgery (1). The editorial particularly highlights the long duration of epilepsy experienced by the patients in the study, before receiving surgery. Very few patients had surgery within the first 10 years of illness. Kwan and Brodie (2) reported that patients for whom even one antiepileptic drug (AED) fails as a result of lack of efficacy have only an 11% chance of becoming seizure free over the subsequent follow-up period of up to 5 years. In light of this fact, early referral for surgery seems appropriate. Surgical intervention is a major undertaking and involves some (although minimal) risk. Patients should be informed that, overall, their chance of *never experiencing another seizure after epilepsy surgery* is approximately 110 in 371, or 30%. Of course, this

incorporates all comers, including those with temporal as well as extratemporal resections. Temporal resections would be expected to have a better overall outcome, although it would be reassuring to confirm this with data.

This type of long-term outcome study is very useful. Similar outcome studies should be performed on patients who become seizure free through other means, such as AED therapy, for whom relapse rates may very well be higher. Only with this information can physicians properly inform their patients.

by Jacqueline A. French, M.D.

References

1. Trevathan E, Gilliam F. Lost years: Delayed referral for surgically treatable epilepsy. *Neurology* 2003;61:432–433.
2. Kwan P, Brodie MJ. Early identification of refractory epilepsy. *N Engl J Med* 2000;342:314–319.