

FIRST RANDOMIZED STUDY OF EPILEPSY SURGERY

A Randomized, Controlled Trial of Surgery for Temporal-Lobe Epilepsy

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BACKGROUND: Randomized trials of surgery for epilepsy have not been conducted, because of the difficulties involved in designing and implementing feasible studies. The lack of data supporting the therapeutic usefulness of surgery precludes making strong recommendations for patients with epilepsy. We conducted a randomized, controlled trial to assess the efficacy and safety of surgery for temporal-lobe epilepsy.

METHODS: Eighty patients with temporal-lobe epilepsy were randomly assigned to surgery (40 patients) or treatment with antiepileptic drugs for one year (40 patients). Optimal medical therapy and primary outcomes were assessed by epileptologists who were unaware of the patients' treatment assignments. The primary outcome was freedom from seizures that impair awareness of self and surroundings. Secondary outcomes were the frequency and severity of seizures, the quality of life, disability, and death.

RESULTS: At one year, the cumulative proportion of patients who were free of seizures impairing awareness was 58 percent in the surgical group and 8 percent in the medical group ($P < 0.001$). The patients in the surgical group had fewer seizures impairing awareness and a significantly better quality of life ($P < 0.001$ for both comparisons) than the patients in the medical group. Four patients (10 percent) had adverse effects of surgery. One patient in the medical group died.

CONCLUSIONS: In temporal-lobe epilepsy, surgery is superior to prolonged medical therapy. Randomized trials of surgery for epilepsy are feasible and appear to yield precise estimates of treatment effects.

didates for surgical treatment, yet only a small fraction of these patients receives presurgical evaluation. Particularly saddening to those working in comprehensive epilepsy centers is the frequently encountered patient, newly referred, who has endured years of poor seizure control even though he or she has an epilepsy syndrome that is surgically remediable with relative ease, such as medial temporal lobe epilepsy.

One reason that general neurologists may be hesitant to refer patients for consideration of surgical treatment may be the lack of “proof” that resective procedures are effective and safe. Until the publication of the article by Wiebe et al., the medical literature was bereft of a clinical trial aimed at assessing in a rigorous manner the efficacy of epilepsy surgery. This report now provides evidence for the superiority of surgical treatment compared with pharmacotherapy alone for the treatment of temporal lobe epilepsy using a prospective, randomized, and controlled study design.

Eighty patients who were 16 years old or older, who had histories suggestive of temporal lobe seizure semiology and who had experienced seizures for at least 1 year, had at least monthly seizures, and had failed a minimum of two antiepileptic drugs were enrolled in the study. These patients also met various exclusion criteria aimed at excluding extratemporal and multifocal syndromes.

Half of the patients were randomly assigned to the surgical group, where they underwent ictal video/surface EEG monitoring within 48 hours of randomization; invasive monitoring was performed if needed. Patients with unilateral or “mostly unilateral” temporal lobe epilepsy who then demonstrated acceptable findings on the intracarotid amobarbital test and concordant magnetic resonance imaging and neuropsychological data, a total of 36, underwent anteromedial temporal lobe resection within 4 weeks of randomization. The remaining 40 patients, randomized to medical treatment, were placed on the institution's “standard” 1-year waiting list for epilepsy monitoring and underwent best medical management. Both groups of patients maintained seizure diaries and were seen every 3 months by epileptologists who were blinded to patient identity and treatment group assignment. Diaries were reviewed, medications were adjusted as needed, and an assessment of quality of life and employment/school status was performed.

The primary outcome measure was freedom from seizures impairing awareness at 1 year of follow-up, measured by the

COMMENTARY

Surgical resection is a grossly underused treatment for medically refractory epilepsy. In the United States alone, 200 to 300,000 patients with intractable epilepsy are potential can-

patient diary report and analyzed using Kaplan-Meier event-free survival curves. Using an intent-to-treat analysis, 58% of patients in the surgical group remained free from events, whereas only 8% in the medical group attained this outcome—a highly statistically significant finding. Secondary measures demonstrated the surgical patients to have a substantially higher rate of freedom from all types of seizure events, a significantly better quality of life, and a trend toward more favorable employment and/or school status. Adverse events in the surgical group included a small thalamic infarct in one patient, an infected wound in one patient, and two patients with a clinically relevant decline in verbal memory. Importantly, although no deaths occurred in the surgical group, one patient in the medical group during the year of the study died of a sudden, unexplained death.

The main deficiency of this study is the limited follow-up period necessitated by the study design. Although 1 year is a

reasonable period to ascertain postoperative seizure freedom in a population of patients previously prone to frequent seizures, the findings in this report cannot be assumed to be identical to longer term outcomes.

This landmark clinical trial is the first to investigate the efficacy and safety of epilepsy surgery using the gold standard for clinical studies: the prospective, randomized, controlled trial. Using this paradigm, the superiority of surgical treatment compared with management, with pharmacotherapy, and the relative safety of epilepsy surgery were clearly demonstrated for patients with uncontrolled temporal lobe epilepsy, at least at 1 year of follow-up. Perhaps this evidence will finally compel the referral of a greater number of patients with uncontrolled epilepsy to consideration for surgical treatment.

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