

FIRST FINDINGS FROM THE MULTICENTER STUDY OF EPILEPSY SURGERY

The Multicenter Study of Epilepsy Surgery: Recruitment and Selection for Surgery

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PURPOSE: Multiple studies have examined predictors of seizure outcomes after epilepsy surgery. Most are single-center series with limited sample size. Little information is available about the selection process for surgery and, in particular, the proportion of patients who ultimately have surgery, and the characteristics that identify those who do versus those who do not. Such information is necessary for providing the epidemiologic and clinical context in which epilepsy surgery is currently performed in the United States and in other developed countries.

METHODS: An observational cohort of 565 surgical candidates was prospectively recruited from June 1996 through January 2001 at six northeastern and one mid-western surgical centers. Standardized eligibility criteria and protocol for presurgical evaluations were used at all seven sites.

RESULTS: Three hundred ninety-six (70%) study subjects had resective surgery. Clinical factors such as a well-localized magnetic resonance imaging (MRI) abnormality and consistently localized EEG findings were most strongly associated with having surgery. Of those who underwent intracranial monitoring (189, 34%), 85% went on to have surgery. Race/ethnicity and marital status were marginally associated with having surgery. Age, education, and employment status were not. Demographic factors had little influence over the surgical decision. More than half of the patients had intractable epilepsy for ≥ 10 years, and five or more drugs had failed by the time they initiated their surgical evaluation. During the recruitment period, eight new antiepileptic drugs were approved by the Food and Drug Administration for use in the United States and came into increasing use in this study's surgical candidates. Despite the increased availability of new therapeutic options, the proportion that had surgery each year did not fluctuate significantly

from year to year. This suggests that, in this group of patients, the new drugs did not provide a substantial therapeutic benefit.

CONCLUSIONS: Up to 30% of patients who undergo presurgical evaluations for resective epilepsy surgery ultimately do not have this form of surgery. This is a group whose needs are not currently met by available therapies and procedures. Lack of clear localizing evidence appears to be the main reason for not having surgery. To the extent that these data can address the question, they suggest that repeated attempts to control intractable epilepsy with new drugs will not result in sustained seizure control, and eligible patients will proceed to surgery eventually. This is consistent with recent arguments to consider surgery earlier rather than later in the course of epilepsy. Postsurgical follow-up of this group will permit a detailed analysis of presurgical factors that predict the best and worst seizure outcomes.

Multicenter Study of Epilepsy Surgery: Initial Outcomes in the Multicenter Study of Epilepsy Surgery

Spencer SS, Berg AT, Vickrey BG, Sperling MR, Bazil CW, Shinnar S, Langfitt JT, Walczak TS, Pacia SV, Ebrahimi N, Frobish D

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OBJECTIVE: To obtain prospective data regarding seizures, anxiety, depression, and quality of life (QOL) outcomes after resective epilepsy surgery.

METHODS: The authors characterized resective epilepsy surgery patients prospectively at yearly intervals for seizure outcome, QOL, anxiety, and depression, by using standardized instruments and patient interviews.

RESULTS: Of 396 patients who underwent resective surgical procedures, 355 were followed up for ≥ 1 year. Of these, 75% achieved a 1-year remission at some time during follow-up; patients with medial temporal (77%) were more likely than those with neocortical resections (56%) to achieve remission ($P = 0.01$). Relapse occurred in 59 (22%) patients who remitted, more often in medial

temporal (24%) than neocortical (4%) resected patients ($P = 0.02$). QOL, anxiety, and depression all improved dramatically within 3 months after surgery ($P < 0.0001$), with no significant difference based on seizure outcome. After 3 months, QOL in seizure-free patients further improved gradually, and patients with seizures showed gradual declines. By 12 and 24 months, overall QOL and its epilepsy-targeted and physical health domains were significantly different in the two outcome groups. (Anxiety and depression scores also gradually diverged, with improvements in seizure-free and declines in continued-seizure groups, but differences were not significant.)

CONCLUSIONS: Resective surgery for treatment of epilepsy significantly reduces seizures, most strikingly after medial temporal resection (77% 1-year remission) compared with neocortical resection (56% 1-year remission). Resective epilepsy surgery has a gradual but lasting effect on QOL, but minimal effects on anxiety and depression. Longer follow-up will be essential to determine ultimate seizure, QOL, and psychiatric outcomes of epilepsy surgery.

COMMENTARY

Clinicians who routinely use epilepsy surgery to treat pharmacoresistant epilepsy know from experience that surgical resection often is effective in abolishing seizures and generally is safe. Indeed, this treatment can lead to renewed lives for many patients previously devastated by uncontrolled epilepsy. Despite the clinical observations regarding the efficacy of resection, the field of surgical epileptology largely is bereft of prospective, large-scale, long-term studies not only to assess the outcomes of resective epilepsy surgery but also to analyze the process by which surgical candidacy is determined.

These companion articles constitute the initial reports of the Multicenter Study of Epilepsy Surgery, an ambitious prospective study of about 400 patients who have been evaluated for and treated with resective epilepsy surgery, by using a standardized protocol and long-term follow-up, at seven epilepsy centers. The article by Berg et al. characterizes the factors associated with surgical candidacy, analyzing the features of patients who ultimately go on to surgical treatment and those who do not. The report by Spencer et al. analyzes the initial outcome of patients followed up postoperatively for ≥ 1 year.

In the article by Berg et al., 396 of 565 eligible patients ultimately underwent resective surgery, but 169 (30%) did not.

Not surprisingly, factors that were most strongly associated with surgery were presence of a focal magnetic resonance imaging (MRI) abnormality and a well-localized scalp EEG focus. The use of new antiepileptic drugs that became available during the time of evaluation, while slightly delaying time to surgery, did not appear to reduce the need for surgery. About half of the patients who did not have surgery were not deemed to be candidates, but a large number (81) of those not operated on withdrew from further evaluation during the course of the study. The authors stated that no information was available to determine why patients ceased participation, but this information would be helpful in understanding the factors that dissuade patients from pursuing presurgical evaluation and surgical treatment. With a better appreciation of these factors, clinicians might be able to develop educational techniques that more effectively increase patient participation in beneficial treatments.

The article by Spencer et al. documents a 75% overall rate of 1-year seizure remission in the nearly 400 patients treated with surgery. Remission was more likely in those requiring medial temporal resections compared with those who had neocortical resections (77% compared with 56%). A relatively high relapse rate (22%) was seen, particularly in those with medial temporal resections. Interestingly, relapse was associated with a putative explanation (e.g., medication reduction) in 80% of patients. It will be intriguing to see in the longer-term follow-up reports what proportion of these individuals obtains recaptured seizure control. In addition to measures of seizure reduction, the authors tracked a number of other measures to assess postoperative outcome. Improvements in quality-of-life measures, although transiently occurring in the short term for all patients, persisted and increased in those patients with the best seizure control. Improvements in postoperative depression and anxiety scores were greatest in those individuals whose seizures remained abolished.

These first reports from the Multicenter Study of Epilepsy Surgery provide initial glimpses into the factors that influence surgical candidacy and clinical outcomes. The uniform protocol applied to the patients at all seven centers allows a confident interpretation of outcomes. None of the findings is particularly surprising, but they reinforce the anecdotal experience of many epileptologists and also provide a more comprehensive and uniform analysis to help inform clinical decision making and patient counseling. The longer-term outcomes will be of particular interest, though, in understanding what is ultimately accomplished with resective surgery—or not—for these patients. The epileptology community eagerly awaits their analysis and publication.

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