

WHEN EPILEPSY SURGERY FAILS . . . THERE IS OFTEN A SECOND CHANCE

Temporal Lobe Epilepsy: Analysis of Failures and the Role of Reoperation

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PURPOSE: To analyze failures and reoperations in temporal lobe epilepsy to compare these patients with those who are seizure free, and to determine any significant differences between the groups.

METHODS: A total of 262 patients with temporal lobe epilepsy, treated surgically between 1984 and 2002, were followed up at 3, 6, and 12 months, and yearly thereafter. Sixty-five percent became seizure free (class I), 19% had rare seizures (class II), and 16% continued to have seizures (classes III and IV). Patients in classes III and IV underwent reevaluation and were compared with seizure-free patients.

RESULTS: Analysis of failures ($n = 41$): 12% had febrile seizures; 29%, head trauma; 7%, encephalitis; 52%, abnormal imaging; 34%, bitemporal spiking; and 20%, posterior temporal localization. Postsurgical MRI (available in 30 of 41 patients) showed residual posterior mesial temporal structures (PMTS) in 86.6%, PMTS and posterior

temporal lesions in 6.6%, and posterior temporal lesions in another 6.6%. Twenty-one had reoperation, 14 had resection of the PMTS, five of the PMTS and basal posterior temporal cortex, and two of the PMTS, and posterior temporal lesions. No surgical mortality or morbidity was found; 57% became seizure free, and 24% had rare seizures. Seizure-free patients ($n = 170$): 45% had febrile seizures; 12%, head trauma; and 70%, abnormal imaging studies.

CONCLUSIONS: When compared with seizure-free patients, patients who failed temporal lobe epilepsy surgery were less likely to have a history of febrile seizures and abnormal imaging, and more likely to have a history of head trauma, encephalitis, and posterior temporal localization, suggesting larger epileptogenic zones. After reoperation, 57% became seizure free. Predictors of a good outcome after reoperation were anterior temporal localization and abnormal imaging studies.

Resective Reoperation for Failed Epilepsy Surgery: Seizure Outcome in 64 Patients

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PURPOSE: To determine the surgical outcome and factors of predictive value in patients undergoing reoperation for intractable partial epilepsy.

METHODS: The authors retrospectively studied the operative outcome in 64 consecutive patients who underwent reoperation for intractable partial epilepsy. Demographic data, results of comprehensive preoperative evaluations, and the seizure and neurologic outcome after reoperation were determined. All patients were followed up for a minimum of 1 year subsequent to their last operative procedure.

RESULTS: Fifty-three patients had two surgeries, and 11 patients had three or more operations. The first surgery involved a lesionectomy ($n = 33$), “nonlesional” temporal lobe resection ($n = 28$), and a “nonlesional” extratemporal resection ($n = 3$). The mean duration between the first and second procedure was 5.5 years. Fifty-five patients underwent an intralobar reoperation, whereas nine had a resec-

tion of a different lobe. After reoperation, 25 (39%) patients were free of seizure, 6 (9%) patients had rare seizures, 12 (19%) patients had a worthwhile improvement, and 21 (33%) patients failed to respond to surgery. Predictors of seizure-free outcome were age at seizure onset older than 15 years ($p = 0.01$), duration of epilepsy 5 years or less at the time of initial surgery ($p = 0.03$), and focal interictal discharges in scalp EEG ($p = 0.03$). By using a logistic regression model, two significant predictors emerged: duration of epilepsy ≤ 5 years (odds ratio, 3.18; $p = 0.04$) and preoperative focal interictal discharge (odds ratio, 4.45; $p = 0.02$). Complications of reoperation included visual field deficits ($n = 9$), wound infection ($n = 2$), subdural hematoma ($n = 1$), and hemiparesis ($n = 1$).

CONCLUSIONS: Reoperation may be an appropriate alternative form of treatment for selected patients with intractable partial epilepsy who fail to respond to initial surgery.

COMMENTARY

Resectiv e epilepsy surgery is currently the most effective overall treatment for patients with pharmacoresistant, localization-related epilepsy, and surgery is the intervention most likely to render such patients free from seizures. Sometimes, though, surgery fails. Learning from these failures—understanding why they occur, how to predict which patients are at greatest risk, how to minimize unsuccessful outcomes, and how to manage disappointing outcomes when they do occur—is one of the most important endeavors facing epileptologists today.

Despite the maturity of the field of surgical epileptology, little analysis of failed epilepsy surgery exists. Perhaps this fact is not too surprising, as much energy has been focused on establishing the efficacy of surgical treatment and conveying to the medical community the urgency of prompt referral for comprehensive evaluation to determine patients' surgical candidacy. The companion articles, highlighted herein, explore surgical failures and report on the outcomes of reoperation for patients in whom the first attempt at surgical treatment was unsuccessful. The report by Siegel et al. emphasizes the role of reoperation across a spectrum of patients, whereas the article by Salanova and colleagues restricts analysis to patients with temporal lobe epilepsy.

Siegel and colleagues retrospectively reviewed their database of nearly 1,500 surgical epilepsy patients treated from 1985 through 2000 to arrive at 64 patients who underwent resective reoperation at the Mayo Clinic. These were patients with medically intractable epilepsy before and after their first resective surgery who did not have a malignant brain tumor as the basis for their seizures and who had at least 1 year of follow-up after their reoperation. The first operation had consisted of temporal resection in 44 patients and extratemporal resection in the remaining 20. After these procedures, 57 patients had experienced seizure recurrence within the first year, whereas the remaining patients had had longer-term remission, averaging 4.6 seizure-free years (range, 2–11 years). In the Siegel series, reoperation took place from 4 months to 23 years after the initial procedure and consisted of lesionectomies, selective hippocampectomies, and corticectomies. Eleven patients went on to an additional third or fourth resection. Histopathologic analysis revealed a spectrum of abnormalities in all but five patients.

Ultimate seizure outcomes after reoperation(s) at mean follow-up time of 4.0 years (range, 1–11 years) were 25 (39%) patients in class I (seizure free), 6 (9%) patients in class II (rare seizures), 12 (19%) patients in class III (worthwhile improvement), and 21 (33%) patients in class IV (no worthwhile improvement). Complications occurred in 13 (20%) patients, with one of these permanent (mild hemiparesis). Logistic regression analysis found only two factors to predict a seizure-

free outcome: duration of epilepsy of less than 5 years at the time of initial surgery and presence of focal interictal epileptiform discharge on preoperative EEG. Several nonsignificant trends also were pointed out by the authors: patients with lesions tended to be more likely to attain seizure freedom than those without (48% vs. 29%); patients who underwent temporal lobe lesionectomy were more likely to become seizure free than were those who underwent extratemporal lesionectomy (63% vs. 35%); and patients who had had temporal resections that included the mesial structures were more likely to be rendered seizure free than were those whose resections did not.

Salanova and colleagues focused their analysis on patients with medically refractory temporal lobe epilepsy who failed to achieve adequate seizure control and compared those patients with individuals who had attained a seizure-free outcome. In addition, this study assessed ultimate outcomes for those who went on to reoperation. The basis for this analysis was 262 consecutive patients with intractable temporal lobe epilepsy operated on by the same surgeon at Indiana University Medical Center between 1984 and 2002. Of these, 41 patients with class III or class IV outcomes were considered surgical failures and formed the cohort for comparative analysis with the group of surgical successes.

In regard to age at seizure onset, age at surgery, mean duration of epilepsy, or surgical pathological diagnosis (even, somewhat surprisingly, presence or absence of mesial temporal sclerosis), patients who failed to benefit significantly from their first operation did not differ significantly from patients who achieved benefit. A number of statistically significant differences between the two groups, however, were found. Patients for whom their first surgery failed were less likely to have a history of febrile seizures, less likely to have abnormal preoperative imaging, more likely to have a history of head trauma, and more likely to have required invasive recordings to localize their seizures. Whereas these features may help in counseling patients as to realistic expectations, their utility is somewhat limited, because not all patients with those risk factors realize a poor outcome. Notably, the late mortality rate for patients for whom their first operation failed was 15%, compared with just 1% for those rendered seizure free.

Twenty-one patients, all with unitemporal localization, went on to reoperation. Of the 20 patients who did not have further surgical treatment, 6 had required invasive recordings before their first surgery (and presumably did not wish to undergo additional invasive procedures to determine their candidacy for reoperation, although this is not stated), 5 had frequent bilateral independent temporal lobe interictal epileptiform discharges, 1 had a widespread epileptogenic zone, and 8, who were potentially good candidates for reoperation, decided against further surgery.

Reoperation occurred between 1 and 11 years after the initial surgery and produced no morbidity or mortality. After reoperation, 12 (57%) of the 21 patients achieved class I outcome; 5 (24%) of 21, class II outcome; 2 (10%) of 21, class III outcome; and 2 (10%) of 21, class IV outcome (the duration of follow-up after the second operation for these outcomes is unclear). The late mortality rate for the 20 patients for whom the initial surgery failed but who did not undergo reoperation was 20%, compared with 10% for those patients who had reoperation and failed to benefit from the second surgery and 0 for those reoperated on who ultimately achieved a seizure-free outcome.

These two retrospective analyses provide significant insight into the quagmire of failed epilepsy surgery. Factors predictive of likelihood of surgical failure include normal imaging and etiologic risks that seem to predispose to widespread epileptogenic zones (e.g., head trauma, encephalitis). It seems prudent in such cases, then, to be especially meticulous in fully defining the area to be resected during the preoperative multimodality evaluation and during intraoperative physiological monitoring. In addition, several common reasons underlie these failures, including lack of complete lesionectomy in those patients with lesional epilepsy, insufficient resection of perilesional epilepto-

genic tissue, and failure to resect mesial temporal structures fully in patients with temporal lobe epilepsy. The practical corollary from these observations is the need to bring to bear procedural approaches, such as intraoperative surgical navigation technology, to enhance the likelihood of complete surgical excision of the intended pathologic tissue.

Most strikingly, both of these reports call attention to the high level of efficacy and safety of reoperation in selected patients. Completing the lesionectomy, expanding the initial zone of resection, or fully resecting mesial temporal structures is more likely than not to transform surgical failures into surgical successes and at low risk. By contrast, the mortality risk associated with ongoing, uncontrolled seizures is once again clear.

These companion articles emphasize the important role that reoperation can play for some patients who have not realized adequate benefit from resective epilepsy surgery. Perhaps these reports will prompt clinicians to consider this option for many patients with less than optimal surgical outcomes. It seems that proactively seeking out these patients and offering comprehensive reevaluation for many of them is in order.

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