Down, But Not Out: Treatment After Ineffective Epilepsy Surgery

Many patients experience significant benefits from epilepsy surgery, but some do not. Here's how the care team can respond to sub-optimal results and plan future therapy.

By John Stern, MD

Surgical treatment of epilepsy requires a multidisciplinary team of caregivers working in conjunction with the patient and his/her family in efforts to attain better control of seizures and an improved quality of life. In many instances, successful surgery results in seizure-freedom with eventual dose reduction or withdrawal of one or more anti-epileptic drugs (AEDs). However, surgery does not always yield a meaningful reduction in seizure frequency for some patients and this usually results in a treatment dilemma.

"Unsuccessful" surgeries such as these can lead to significant frustration on the part of patients, their families, as well as the members of the treatment team. Faced with suboptimal results, the neurologists, neurosurgeons, nurses, and others who work

with patients throughout the process of referral, evaluation, surgery, and post-operative care all must come to a decision about the best "next steps," while working to address the patients' numerous concerns post-surgery.

Following are some considerations to guide neurologists and other members of the care team in making therapeutic decisions and counseling patients following sub-optimal surgical treatment.

Failure of Surgery Does Not Mean Surgery Is Wrong

The data clearly support the role of epilepsy surgery as a therapeutic option for appropriate patients. A study published last year compares a series of patients who underwent epilepsy surgery an average of about 15 years earlier to a matched patient series with medication refractory epilepsy that was not treated surgically. The epilepsy surgery patients had fewer seizures, used less antiepileptic medication, and had better Health-Related Quality of Life (HRQoL) in several dimensions of the Quality of Life in Epilepsy Inventory 89 instrument although there was possibly a slight disadvantage in the language dimension among those patients with seven years of follow-up or less.[1] Nearly half (48 percent) of surgery patients were seizure free during the previous year versus just 19 percent of the non-surgical control group, and only 70 percent of the surgery group used AEDs, compared to 93 percent of controls.

A systematic meta-analysis of the literature also supports the long-term benefits of surgery.[2] It found that the median proportion of long-term seizure-free patients was 66 percent with temporal lobe resections, 46 percent with occipital and parietal resections, and 27 percent with frontal lobe resections.

Surgery also can produce an improvement in quality of life (QOL). When comparing Quality of Life in Epilepsy Inventory-89 (QOLIE-89) scores before surgery, within six months, and roughly each year for the next three years among 396 patients undergoing resective epilepsy surgery, researchers found significant increases in QOL scores at the first post-operative assessment. Subsequent improvements in QOL were associated with seizure- and aura-freedom.[3]

Overall, the benefits of surgery for some patients are clear, which indicates that surgery should be considered for all patients who have medication refractory epilepsy. However, the failure of surgery for some patients is an unfortunate reality that needs to be confronted clinically with the patient and through additional research toward improving surgical success. In both settings, the failure can be an opportunity, albeit drastic, for insights that may benefit others with epilepsy and the individual patient. Others benefit when the experience leads to better prognostication for surgical outcome, an important aspect of all surgical care. The individual patient benefits if the apparent reason for surgical failure leads to a treatment that ultimately improves seizure control. Combined, these challenges in managing disappointing surgical outcomes present crucial issues for today's epileptologists.

The Case for Re-operation

Sometimes, a repeat surgical evaluation after surgical failure leads to consideration of another operation. Such experiences have been documented in publications such as one by Wyler et al.[4] in 1989. The report describes 37 patients who had ineffective epilepsy surgery and were re-evaluated with MRI and long-term scalp electroencephalographic monitoring and then were found to be candidates for reoperation. The repeat surgeries involved focal resections after initial focal resections in 30 cases, stereotactic lesionectomy in one case, or focal resections following anterior corpus callosotomy in six cases. The authors found that "patients with initial focal resections followed by enlargement of the original operative site had the most successful outcome, especially those with complex partial seizures of temporal lobe origin."

When the original operation was for mesial temporal lobe epilepsy, the most common cause for poor outcome was insufficient hippocampal resection. The patients most likely to benefit from reoperation were: "1) those with initially incompletely resected structural lesions; 2) those who underwent further resection of the initial operative site rather than resection of a different cortical region, and 3) those who were initially evaluated with invasive ictal monitoring." The third finding supports consideration of reoperation even for some of the diagnostically challenging patients.

Siegel et al.[5] emphasized the function of reoperation across a spectrum of patients. They found that reoperation may be an appropriate alternative form of treatment for selected patients with intractable focal epilepsy who failed to respond to initial surgery. The authors retrospectively studied the operative outcome in 64 consecutive patients for a minimum of one year subsequent to their last operative procedure, of whom 53 had two operations, and 11 had three or more operations. The mean duration between the first and second procedure was 5.5 years.

Following their reoperation, 25 patients (39 percent) were seizure-free, 6 patients (9 percent) had rare seizures, 12 patients (19 percent) had a "worthwhile" improvement, and 21 patients (33 percent) failed to respond to the reoperation. A logistic regression model showed two significant predictors: duration of epilepsy ≤5 years (odds ratio, 3.18; $p = 0.04$) and preoperative focal interictal epileptiform discharges (odds ratio, 4.45; $p = 0.02$).

While Siegel et al. were broad in their inclusion criteria, Salanova et al.[6] limited analysis to patients with temporal lobe

epilepsy who failed to achieve sufficient seizure control. Their analysis includes a valuable consideration of factors that were associated with attaining seizure-freedom after the initial operation and also factors related to successful reoperation. Twenty-one patients, all with unitemporal localization, went on to reoperation. Another 20 patients did not have further surgical treatment related to a variety of circumstances; six required invasive recordings before their first surgery, five experienced frequent bilateral independent temporal lobe interictal epileptiform discharges, one had a widespread structural abnormality, and eight, who were thought of as candidates for reoperation, opted against it.

Of those who chose another surgery, 14 had resection of the posterior mesial temporal structures (PMTS), five of the PMTS and basal posterior temporal cortex, and two of the PMTS and posterior temporal lesions. No surgical mortality or morbidity occurred and 57 percent became seizure free, while 24 percent had rare seizures. The results from this collection of publications support consideration of reoperation with a perspective similar to the recommendations for initial epilepsy surgery when medications fail. That is, reoperation benefits some patients and determining which patients requires detailed diagnostic testing. The key difference is that the reoperation patients already underwent an evaluation, but case series evidence supports re-evaluation nevertheless.

The Case for Re-Diagnosis

Another benefit of re-evaluation is the characterization of the seizures that continue after epilepsy surgery. An ideal surgical evaluation includes recording multiple occurrences of each of the patient's habitual seizures to determine whether more than one epileptogenic focus is likely to be present and to exclude the possibility that non-epileptic seizures also are present. An important question to ask early after surgical failure is whether the seizures that persist are the same as those that preceded surgery and the same as ones recorded during the evaluation. Occasionally, patients develop an entirely new type of seizure after surgery. Indication that the evaluation did not include the persisting seizure re-introduces the diagnostic questions that the initial evaluation sought to settle. Specifically, is the persisting seizure epileptic and, if so, is it arising from the same anatomic region? Only video-electroencephalographic monitoring can answer these questions. When the monitoring identifies non-epileptic seizures or a second region likely to be epileptogenic, an explanation for the surgical failure is apparent and the next step in treatment is clear. As such, repeat monitoring is highly valuable for both medical decision making and explaining failure to both the patient and the caregiving team.

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Epilepsy surgery sometimes can change seizure manifestation. A decrease in seizure frequency, and sometimes severity, may result from incomplete resection of an accurately localized epileptogenic zone, which, of course, is helpful information when considering reoperation with extension of the resection. A change in actual aura or ictal behavior may indicate an impact on the seizure's propagation without fully affecting the epileptogenic zone, which is less promising than a decrease in severity but still helpful when planning reoperation. An entirely new type of seizure also can indicate the development of non-epileptic spells. This disorder, which patients with medication refractory epilepsy are at risk for developing, may be related to the stresses of recovery or other factors needing the intervention of a psychiatrist or psychologist.

Working with the Patient

Clearly, establishing appropriate expectations prior to surgery is critical. Patients and families must fully understand the risks and benefits of surgery, including the likelihood seizure-freedom, seizure-improvement, and complications. Of course, the nature of the complications and their possible impact on daily life needs to be described in detail. However, the most often overlooked component of setting expectations is a discussion of the impact of improved seizure control on daily life. Patients and their families should have a realistic expectation of how life may be different if seizures are eliminated. Expectations for a sudden change in outlook or social circumstances are not nearly as realistic as a change in employability and mobility.

However, even employability may not change as immediately as expected if the patient has not been in the workplace recently, or ever. As such, discussing the personal reasons for epilepsy surgery will decrease the likelihood of disappointment, which can occur even when a patient becomes seizure free. Avoiding such disappointments is another way to decrease the likelihood of "surgical failure," because surgical failure sometimes can still occur even when seizure-freedom has been achieved.

In the aftermath of a "failed" epilepsy surgery, patients may be emotionally charged. A resection is a significant operation, associated with notable pre-operative anxiety. Following failed surgery, there may be disappointment, regret, and even a tendency to minimize the impact of the experience out of concern that failure may negatively impact the attention provided by the caregiving team. Maintaining consistent medical attention in the face of patient and caregiver disappointment is essential.

Assessing the consequences of surgery and options for moving forward requires sensitivity to the patient's needs and concerns, an openness to new therapeutic options, and a frank discussion of all actions taken thus far and available moving forward. The first step is to discuss previous treatments and how each failed. However laborious, this step-by-step re-examination is helpful toward identifying treatment options that were previously not considered.

Surgery continues to be the best prospect to control seizures for patients with medication-refractory focal epilepsy. This is especially important to recognize as true despite the increasing number of mechanistically unique AEDs that are now available and the continued underuse of surgery. However, epilepsy surgery requires what is arguably one of the most demanding in detail and precision of all evaluations in medicine. The surgical results show the signatures of a collaborating, multidisciplinary team of neurologists, neurosurgeons, neuroradiologists, neuropsychologists, EEG technologists, specialist nurses, and others. Beyond individual patients, the hope is that the continued and focused application of this talent pool will lead us to improved surgical outcomes, even for patients for whom epilepsy surgery currently is failing. **PN**

John Stern, MD is Associate Professor of Neurology at the David Geffen School of Medicine at University of California, Los Angeles. He is on staff in the Seizure Disorder Center at UCLA Health System.

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