

## Editorial

# Cut It Out: The Case for Earlier Referral for Resective Epilepsy Surgery

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## EDITORIAL

Epilepsy is one of the most commonly encountered neurologic disorders. This condition, in which patients have an enduring predisposition to future unprovoked epileptic seizures, is estimated to affect 50 million people worldwide. Approximately 10% of individuals will experience a seizure at some point in their lifetimes. When such seizures are uncontrolled, they have the potential to delay development, impair cognitive functioning, negatively affect psychosocial functioning, lead to significant injury, and even increase the risk of death. Fortunately, the majority of patients with epilepsy can achieve seizure cessation with antiepileptic drugs (AEDs). Almost 70% of patients initiated on AEDs can ultimately experience seizure freedom. This includes approximately 50% of patients following initiation of the first AED, with an additional 13% becoming seizure free with a second AED [1].

Unfortunately, approximately 1 in 4 patients with epilepsy will not achieve seizure freedom with medications alone. Such patients, despite compromising less than 25% of those with seizures, account for 80% of the cost of epilepsy in the United States [2]. By the time a third AED is tried, the chance of achieving seizure cessation falls to only 5%. This continues to precipitously drop as more and more AEDs are prescribed. Such patients are often prescribed 3, 4, or even 5 (or more) concurrent AEDs without the realistic expectation of seizure freedom. Rather, such combinations are more likely to result in significant side effects, including increased risk of sedation, cognitive slowing, interactions with other medications, and potentially even a paradoxical increase in seizure frequency [3]. Although physicians prescribing such combinations are only trying to help their patients, they unfortunately may only contribute to worsened quality of life. For some patients, the toxicity of irrational polytherapy may be worse than the disease itself.

For patients with drug resistant focal onset seizures, resective epilepsy surgery (RES) has been shown to be an effective alternative to continued AED trials. Two randomized controlled trials have demonstrated the superior efficacy of RES for medically intractable temporal lobe epilepsy (TLE) versus continued medical management alone [4,5]. In select patients with TLE, rates of seizure freedom may exceed 70% [5].

Although not as dramatic as the rates observed following RES for TLE, the rate for seizure freedom following extratemporal resections is still vastly superior to a third AED. This includes freedom from disabling seizures in 46% of patients following parietal and occipital resections and 27% following frontal lobe resections [6]. Beyond seizure freedom, RES has the potential to significantly increase quality of life, cognitive functioning, and social adaptation [5].

In 2003, the American Academy of Neurology (AAN), in association with the American Epilepsy Society (AES) and the American Association of Neurological Surgeons (AANS), published a practice parameter on the treatment of drug resistant epilepsy with RES [7]. This practice parameter advocated for the referral of patients who did not respond to appropriate trials of first-line AEDs to comprehensive epilepsy centers for possible RES. Unfortunately, this did little to change the pattern of referrals to such centers. Despite evidence of the efficacy of RES for drug resistant focal onset seizures being in the literature for decades, primary care physicians and general neurologists are often too hesitant to make such referrals. It is estimated that only a minority of patients with drug resistant epilepsy ultimately make their way to comprehensive epilepsy centers. Even following the publication of the AAN practice parameter, little appeared to change. No difference in the duration of epilepsy diagnosis to referral or age at the time of referral could be discovered [8]. If anything, patients tended to be older (37 years versus 34.1 years) and had to wait longer for a comprehensive evaluation (18.6 years versus 17.1 years) following publication of the practice parameter [8].

The reasoning for such a continued delay has yet to be fully elucidated. Although some of the delay undoubtedly stems from lack of knowledge of RES, this cannot fully explain the situation (particularly given the lack of improvement following publication of the AAN practice parameter). Rather, it is likely that some of the delay is secondary to physician's erroneous perceptions of what comprehensive epilepsy centers can offer. There is a false perception that such centers like to cut and not much else. When faced with patients with medically intractable seizures that are presumed to be of generalized onset, many clinicians believe there is nothing left to do outside of prescribing yet another

AED. Although unspoken, there may be the fear that referring such patients to comprehensive epilepsy centers will result in no appreciable changes in management other than the transfer to all future care from the generalist to the subspecialist.

The above could not be further from the truth. All patients, regardless of whether or not their medically intractable seizures are focal or generalized in onset, deserve a comprehensive epilepsy center evaluation. Patients who are presumed to have generalized onset seizures may actually have focal onset seizures with quick secondary generalization, making them potential RES candidates. Even the presence of generalized interictal epileptiform discharges on EEG cannot preclude an ultimately successful resective surgery in select patients undergoing a surgical workup [9]. Conversely, patients who are found to not be candidates for RES can still be assisted by the additional resources available at comprehensive epilepsy centers. Such centers are more likely to discuss alternatives to medications such as vagus nerve stimulation (VNS) and the ketogenic diet. In addition, such centers can offer nonsurgical patients earlier access to experimental devices such as trigeminal nerve stimulation (TNS), deep brain stimulation, and responsive neurostimulation. Although such therapies may not promise seizure freedom, they have the potential to improve seizure control without the side effects of AED polytherapy, improving overall quality of life. Given this, it is the duty of all concerned epileptologists, general neurologists, general practitioners, and patients to speak out regarding the necessity of early referral to comprehensive epilepsy centers. We have amazing tools at our disposal; it's about time we shared them with everyone who needs them.

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