

The next level of care in epilepsy

Delays, more delays, delays everywhere

Selim R. Benbadis, MD, and Jerome Engel, Jr., MD, PhD

Neurology: Clinical Practice August 2019 vol. 9 no. 4 284-285 doi:10.1212/CPJ.0000000000000625

Surgical treatment for drug-resistant epilepsy remains underused in the industrialized world; it is estimated that, in the United States, less than 1% of patients with drug-resistant epilepsy, defined as failure of 2 appropriate trials of antiseizure drugs,¹ are referred to an epilepsy center.² Furthermore, when patients are referred, the delay from onset of epilepsy is 18–22 years,^{2,3} often too late to prevent irreversible social and psychological disabilities.

Surgery has been an accepted and effective treatment for certain types of drug-resistant epilepsies for over a century, but for most of the time, it had been considered a luxury afforded only by high-income countries. Advances in diagnostic technology, however, particularly the advent of MRI, have considerably leveled the playing field; a number of countries with limited resources now offer surgical therapy as a cost-effective approach for appropriately selected patients when pharmacotherapy fails.² In this issue of *Neurology: Clinical Practice*, Asranna et al.⁴ review referral patterns to a surgical center in southern India over 2 decades and report an average delay of 18 years that has remained constant over this period of time. This figure is noteworthy because of its striking similarity to the delay of 18–22 years for referral reported in the United States.^{2,3}

The delay to surgical referral in the United States is accompanied by a relatively recent overall decrease in total referrals experienced by many surgical centers.^{5,6} In particular, this reflects a decrease in referral of patients with mesial temporal lobe epilepsy (MTLE), the most common condition treated surgically. A similar referral pattern has been seen in Europe as well.⁶ It has been suggested by some⁶ that both of these phenomena reflect a marked reduction in the pool of patients with drug-resistant MTLE, i.e., that this patient population has been “fished out.” At least as far as delay to referral is concerned, the article by Asranna et al.⁴ is a strong argument against this view. Most of their patients had MTLE, and a subset analysis revealed the same pattern of delay. India’s population is 1.3 billion, over 4 times that of the United States, so there are many more patients with MTLE in India. Furthermore, India has fewer resources than the United States where there are 188 level 4 centers according to the National Association of Epilepsy Centers. Therefore, delay to referral is not because of the lack of surgical candidates in India; their population of patients with drug-resistant MTLE has by no means been “fished out.” Nor is this likely to be the case in the United States if less than 1% of drug-resistant patients are referred to epilepsy centers—the size of the overall population cannot be inferred from this infinitesimally small percentage seen at epilepsy centers.

One possible alternative explanation for the apparent selective decrease in surgical referrals of patients with MTLE is that there is a reduction of referrals overall, but because of MRI identification of small resectable lesions and increasing interest in pediatric epilepsy surgery, both of which usually result in neocortical resections, the greater reduction in MTLE is merely relative. It would appear, therefore, that these patterns reflect a general reluctance on the part of neurologists to refer their patients for surgery.^{2,3}

As a possible solution, Asranna et al. suggest a multipronged strategy to increase awareness among practitioners, but this approach has not worked in the United States. Failure to refer to surgery

Correspondence

Dr. Benbadis
sbenbadi@health.usf.edu

RELATED ARTICLE

Referral trends for temporal lobe epilepsy surgery between 2000 and 2014 in India

Page 297

Department of Neurology (SRB), University of South Florida and Tampa General Hospital, Tampa, FL; and Departments of Neurology (JE), Neurobiology, and Psychiatry and Biobehavioral Sciences, and the Brain Research Institute, David Geffen School of Medicine at UCLA, Los Angeles, CA.

Funding information and disclosures are provided at the end of the article. Full disclosure form information provided by the authors is available with the full text of this article at Neurology.org/cp.

persists, and appears to be worsening, despite: the official International League Against Epilepsy definition of drug-resistant epilepsy¹; 3 randomized controlled trials (RCTs) confirming the safety and efficacy of surgery²; an American Academy of Neurology (AAN) practice parameter recommending surgery as the treatment of choice for drug-resistant MTLE⁷; and AAN Quality Measures that specifically establish referral of patients with drug-resistant epilepsy to an epilepsy center every 2 years as the standard of care.⁸ The failure of expert opinion and definitive data to influence referring neurologists is further documented by 2 studies that found the delay to referral, after the AAN Practice Parameter and first RCT, to be the same as before.^{9,10}

It is true that some forms of surgically remediable epilepsy, particularly MTLE, are initially drug responsive. One study found it took an average of 9 years to become drug-resistant¹¹; however, this does not explain referral delays of 18 years or more, which appears, as Arsanna et al. suggest, to be a global phenomenon. Why are neurologists not referring all patients with drug-resistant epilepsy to epilepsy centers, and when they do refer, why do they wait so long? There are no limits to possible reasons, ranging from inadequate availability of epilepsy surgery centers to inadequate understanding of the role of surgical therapy for epilepsy.^{2,3} Delay to surgery, however, is a longstanding issue that likely reflects 2 larger problems, inappropriate acceptance of incomplete seizure control and reluctance to seek more expert consultation, on the part of both patients and their treating physicians.

Rather than advocating for referral “for surgery,” which can raise a red flag for patients and their neurologists, it is more reasonable to recommend that all patients who fail 2 trials of antiseizure drugs deserve a consultation with a team of multidisciplinary epilepsy specialists at a full-service epilepsy center as the standard of care (i.e., adherence to the AAN quality measures). These centers offer much more than surgery, including more definitive diagnosis of epilepsy type and underlying causes, differential diagnosis of nonepileptic seizures, consideration of a number of nondrug treatments, experimental trials, and psychosocial support services. Approaches to

ensure that all patients with drug-resistant epilepsy have the opportunity for a timely consultation at a full-service epilepsy center should begin with a concerted effort to define the pervasive obstacles to appropriate referral.

Author contributions

S.R. Benbadis and J. Engel: drafted and revised the manuscript.

Acknowledgment

The original work by JE was supported by grants NS002808, NS015654, NS042372, NS033310, NS080181, NS100064.

Study funding

No targeted funding reported.

Disclosure

The authors report no disclosures relevant to the manuscript. Full disclosure form information provided by the authors is available with the full text of this article at Neurology.org/cp.

References

1. Kwan P, Arzimanoglou A, Berg AT, et al. Definition of drug resistant epilepsy: consensus proposal by the ad hoc Task Force of the ILAE Commission on Therapeutic Strategies. *Epilepsia* 2010;51:1069–1077.
2. Engel J Jr. What can we do for people with drug-resistant epilepsy? The 2016 Wartenberg Lecture. *Neurology* 2016;87:2483–2489.
3. Benbadis SR, Heriaud L, Tatum WO, Vale F. Epilepsy surgery, delays and referral patterns—are all your epilepsy patients controlled? *Seizure* 2003;12:167–170.
4. Asranna A, Menon R, Radhakrishnan A. Referral trends for temporal lobe epilepsy surgery between 2000 and 2014 in India. *Neurol Clin Pract* 2019;9:297–303.
5. Englot DJ, Ouyang D, Garcia PA, Barbaro NM, Chang EF. Epilepsy surgery trends in the United States, 1990–2008. *Neurology* 2012;78:1200–1206.
6. Jehi L, Friedman D, Carlson C, et al. The evolution of epilepsy surgery between 1991 and 2011 in nine major epilepsy centers across the United States, Germany, and Australia. *Epilepsia* 2015;56:1526–1533.
7. Engel J, Wiebe S, French J, et al. Practice parameter: temporal lobe and localized neocortical resections for epilepsy: report of the quality standards subcommittee of the American Academy of Neurology, in Association with the American Epilepsy Society and the American Association of Neurological Surgeons. *Neurology* 2003;60:538–547.
8. Fountain NB, Van Ness PC, Bennett A, et al. Quality improvement in neurology: epilepsy update quality measurement set. *Neurology* 2015;84:1483–1487.
9. Haneef Z, Stern J, Dewar S, Engel J Jr. Referral pattern for epilepsy surgery after evidence-based recommendations: a retrospective study. *Neurology* 2010;75:699–704.
10. Choi H, Carlino R, Heiman G, Hauser WA, Gilliam FG. Evaluation of duration of epilepsy prior to temporal lobe epilepsy surgery during the past two decades. *Epilepsy Res* 2009;86:224–227.
11. Berg AT, Langfitt J, Shinnar S, et al. How long does it take for partial epilepsy to become intractable? *Neurology* 2003;60:186–190.