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REVIEW ARTICLE

Clinical guideline: pre-operative evaluation of epilepsy surgery

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Abstract

Epilepsy surgery is an approved treatment for the management of drug-resistant epilepsy or refractory epilepsy (RE). Approximately one-third of patients with epilepsy will develop RE. RE is considered a serious public health threat carrying important biopsychosocial consequences including seizure-related accidents, professional limitations, and increased risk of sudden death. Epilepsy surgery is associated with seizure remission in approximately 65% of patients after a 5 year follow-up. Patients with drug-resistant epilepsy should be referred to a specialized center for a pre-operative evaluation. Pre-operative evaluation requires at least a detailed clinical analysis, an electroencephalogram (EEG) and video-EEG, a cranial magnetic resonance imaging test, as well as neuropsychological, developmental, and psychiatric evaluations. The most common surgical procedures are temporal lobe resections, extratemporal and multilobar resections, lesionectomy, hemispherectomies, callosotomies, and multiple subpial transections, in descending order of frequency.

Key words: *Surgery. Epilepsy. Pre-operative evaluation.*

Introduction

Epilepsy surgery is an approved treatment for the management of drug-resistant or refractory epilepsy (RE)[1-3].

RE is responsible for approximately 80% of the direct and indirect annual costs attributed to epilepsy[4]. The majority of surgical candidates are referred for surgery on average 20-25 years after their initial diagnosis, at which time their prognosis is less favorable.

When do patients with epilepsy require surgical treatment?

According to the criteria established by International League Against Epilepsy (ILAE), approximately 17-33% of patients with epilepsy develop RE throughout the course of the disease (level of evidence III)[5]. A variable portion of patients are able to achieve seizure remission through epilepsy surgery, depending on the type of crisis, underlying pathologies, and the type of series consulted.

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Surgery generates significant improvements in the patients' behavior, cognition, and quality of life and the cost effectiveness of epilepsy has been demonstrated in pediatric as well as adult patients[6].

Early identification of patients with RE that meet criteria for epilepsy surgery candidacy optimizes seizure control and reduces cognitive long-term adverse effects[7]. The age at the time of surgery has been identified as an important modulator of the patients' capacity for cognitive reserve, where the most unfavorable results are in patients with prolonged RE[5,8].

In 2003, the American Academy of Neurology published recommendations for the surgical management of epilepsy in adults. Clinical trials demonstrated that patients with focal epilepsy in the temporal lobe, with or without evolution to bilateral tonic-clonic seizures, who develop resistance to first-line pharmacological treatment must be examined as surgical candidates (considering the new classification of seizures, previously cited in 2003, as incapacitating complex partial seizures, and with or without progression to generalized seizures)[9].

Recommendation	Level of recommendation
Patients with temporal lobe focal epilepsy, with or without progression to bilateral tonic-clonic seizures, who develop resistance to first-line pharmacological treatment, must be examined as surgical candidates (AAN)	A

Studies with 5 year follow-up showed that surgery achieved seizure remission in 65% of cases[10,11].

All subjects with RE must be submitted to a preoperative evaluation to identify or discard well-circumscribed epileptogenic zones (EZ) and assess the potential benefit of a neurosurgical procedure[7].

Patients must meet certain requirements to be considered candidates for epilepsy surgery; the following criteria are indispensable:

1. Confirmed diagnosis of ER
2. A systematic pre-operative evaluation with specific and staggered stages that discard an epileptogenic zone susceptible to surgical resection without provoking major neurological deficits. Published studies lack a comparative analysis of pre-operative algorithms. The specialist consensus is that it must include a rigorous stratified outline followed by a multidisciplinary team that includes a neurologist sub-specialized in epilepsy, a neurophysiologist electroencephalographist, neuroradiologist, neuropsychologist, neuropsychiatrist, and neurosurgeon trained in epileptic surgery procedures. The pre-operative evaluation is carried out in congruent and concurrent stages. The evaluation of each neurological subspecialty has independent value in localizing potential EZ, which is an indispensable objective of the pre-operative evaluation as well as post-operative care. Even when the EZ cannot be outlined or resected due to its location on or nearby a functional or eloquent area of the brain cortex, it is important to consider that a thorough pre-operative evaluation is highly valuable in offering a meaningful diagnosis or prognosis to the patient, as well as guiding alternative therapeutic measures.

Epilepsy surgery is defined as any neurosurgical intervention with the objective of improving the quality of life through the control of epileptic seizures (ES) with minimum secondary side effects[7].

Can epilepsy develop resistance to pharmaceutical treatment?

Epilepsy affects approximately 70 million people worldwide[12,13]; one-third of this population develops RE[5]. In these cases, epilepsy surgery has the potential to eliminate recurrence of ES and improves quality of life[1,14]. Certain epileptic syndromes present better prognosis with surgical treatment when compared to pharmaceutical treatment alone. It is not easy to predict which patients will develop resistance to pharmaceutical treatment; the probability of developing RE varies according to the type of epileptic syndrome and the etiology, this last factor being the most consistently reported in trails predicting the prognosis of epilepsy. The prevalence of RE is higher among patients with symptomatic or cryptogenic epilepsy compared to those with idiopathic epilepsy. A trial including 2200 patients studied for a period between 1 and 7 years, achieved complete control of ES in 82% of patients with generalized idiopathic epilepsy, 45% of cryptogenic focal epilepsy, and 35% of symptomatic focal epilepsy. Another negative factor for the development of RE is an early age of onset. A significant amount of patients with RE also presents hippocampal sclerosis, malformations of cortical development, and dysembryoplastic neuroepithelial tumors.

Temporal lobe epilepsy (TLE) is the most common cause of focal RE[15,16]; therefore, the most frequent type of epilepsy surgery on adults are temporal lobe resections (level of evidence: class I, compared to continuous pharmaceutical treatment alone)[2,17].

Different definitions of RE have emerged throughout the years where multiple factors have been taken into account, such as diagnostic certainty, the number of failed anti-epileptic drugs (AEDs) attempted for seizure control, the frequency of seizures, and other aspects relating to the time span of the seizure pattern. In fact, different terms have been established, such as untreatable epilepsy, uncontrollable epilepsy, difficult to control epilepsy, resistant to pharmaceutical treatment, or RE. Terminology diversity and the lack of definition of specified criteria to conceptualize RE, complicates the comparison of studies and series, thus rendering incomplete conclusions regarding the epidemiology, diagnosis, management, and treatment of RE. The ILAE is the association responsible for establishing a structured definition applicable for both clinical practice and scientific research of RE. Thus, RE was defined as the sustained failure or the lack of ES remission, despite adequate attempts with at least two first-line AEDs as monotherapy or combined therapy that is well tolerated by the patient and was administered in their appropriate corresponding dosages[5]. ES remission or sustained seizure termination was defined as the absence of seizures for at least 12 months or for a period 3 times greater than the longest period of ES remission[5]. This definition may be used to justify a complete evaluation within a epilepsy center, to establish a pre-operative evaluation for epilepsy surgery or to design a randomized controlled trial for AED or other research purposes, thus emphasizing the importance of encouraging the connection between clinical practice and research scientists with a unified epilepsy criteria, obtained through consensus and endorsed by the ILAE.

For patients to be considered surgical candidates for epilepsy surgery, adults must present confirmed diagnosis of RE for at least 2 years; however, in life-threatening situations, this required interval may be less. In pediatric patients, the required interval is <2 years, due to the potential long-term effects that ES can have if present during important stages of neurodevelopment[10].

Candidates for epilepsy surgery are usually between 1 and 60 years of age; however, there are no defined age limits[5,10,14]. According to the Andalusian Epilepsy Guide of 2015[7], surgical candidate selection criteria include:

a. Confirmed diagnosis of RE. Epilepsy that is not controlled with AED after 2 years. Unsuccessful treatment after prescribing two AEDs with adequate dosage respective to each type of ES and adequate treatment compliance. Patient under 2 years of age. High risk of presenting adverse effects on several AEDs.
b. Presence of a single, unilateral, and excisable structural brain lesion.
c. Presence of a non-resectable epileptogenic zone. If a non-excisable zone is identified, neurosurgical techniques such as disconnection procedures, vagus nerve stimulation (VNS), or deep brain stimulation (DBS) are recommended if surgery is considered to reduce the severity of epilepsy and the procedures' side effects are considered acceptable.
d. Presence of psychological or psychiatric comorbidities.
e. Presence of diagnostic doubt, regarding etiology, or epileptic syndrome.
f. Positive patient motivation to accept pre-operative evaluation procedures, surgical intervention, and follow-up protocol.
g. Age, psychiatric pathology, or disabilities are not contraindications for surgical candidacy; however, they must be analyzed on an individual basis[11].

What are the characteristics of patients that are submitted to surgical treatment?

Patients that must be submitted to epilepsy surgery are: (a) those that present refractory ES, (b) patients with physical disabilities due to uncontrolled seizures, and (c) patients with focal RE, low morbidity risk, and potential for rehabilitation and social integration.

A randomized control study demonstrated the superiority of surgical treatment over continuous pharmacological treatment in patients with refractory TLE. 80 patients with mesial temporal lobe sclerosis (mTLS) where randomly distributed into groups of pharmacological or surgical treatment, respectively, after a pre-operative evaluation. Authors discovered that 58% of patients in the surgical group presented seizure remission for 1 year compared to 8% of the patients in the pharmacology group ($p < 0.001$). Authors also found that patients in the surgical group demonstrated better quality of life when compared to the pharmacology group, as measured by reduced work or school absences. In addition, one death was reported within the pharmacology group compared to no deaths in the surgical group[2]. Epilepsy surgery has curative potential when an epileptogenic lesion or zone is completely excised. In other situations, surgery will only serve a palliative function as is the case for the DBS or colostomy procedures for atonic seizures in patients with Lennox-Gastaut syndrome. The curative potential of surgery is maximized with complete excision of a primary cerebral tumor, vascular malformation, malformation of cortical development, or mTLS[18].

Extratemporal epilepsy surgeries are significantly less frequent in surgical series because they represent a greater surgical challenge; they require frequent evaluation through multimodal imaging tests or invasive monitoring. In addition, the EZ in extratemporal epilepsy are more commonly diffuse and poorly circumscribed, they present a faster rate of extension in the seizure propagation and superposition with eloquent areas, thus frequently requiring invasive monitoring to locate the epileptogenic zone(s)[19]. There lacks sufficient evidence to provide definite recommendations for extratemporal epilepsy surgeries in patients without defined lesions or in symptomatic patients with poorly circumscribed lesions. A meta-analysis published by Téllez-Zenteno[11] reported a 60% and 35% remission rate in extratemporal and non-defined lesion epilepsies, respectively.

Which epileptic syndromes should be managed with surgical treatment?

Epileptic syndromes that should be managed by surgery include:

a. Mesial temporal epilepsy.
b. Neocortical epilepsy with a single well-defined lesion without compromise of other eloquent areas of the brain.
c. Hemispheric epilepsy syndromes such as hemimegalencephaly (HME), Sturge-Weber syndrome, Rasmussen's encephalitis, and other unilateral hemispheric lesions.

Patients that generally do not require invasive procedures include:

a. Mesial temporal epilepsy associated with hippocampal sclerosis
b. Circumscribed epileptogenic lesions including benign neoplasias such as ganglioma, dysembryoplastic neuroepithelial tumors, low-grade astrocytoma, oligodendroglioma, vascular malformations, and atrophic brain lesions.
c. Hemispheric lesions, hemiplegic hemiconvulsive epilepsy such as Sturge-Weber syndrome, HME, and Rasmussen's encephalitis.
d. Epileptic encephalopathies and multifocal diseases such as Lennox-Gastaut Syndrome.

Patients that require functional neuroimaging/mapping and/or invasive tests include:

e. Dual pathologies with discordant electroclinical, bilateral mesial temporal sclerosis, poorly circumscribed epileptogenic lesions, malformations of cortical development with normal magnetic resonance imaging (MRI) in or near eloquent areas.

What are the primary modalities of surgical treatment?

Modalities of resection include techniques where the EZ are excised without producing a significant functional deficit. In addition, there are modalities of non-resection techniques including disconnection or palliative procedures[3]. The most frequently performed procedures are temporal lobe resections, extratemporal and multilobar resections, lesionectomy, hemispherectomy, callostomies, and multiple subpial transections[7].

a. Anterior temporal lobectomy or anterior medial temporal resection: it is the most commonly practiced procedure consisting of the excision of medial temporal structures (amygdala, hippocampus, and parahippocampal gyrus), up to 6 cm of anterior temporal lobe cortex in the non-dominant hemisphere and up to 4.5 cm in the dominant hemisphere. To avoid neuropsychological side effects and superior quadrantanopsia, the resection of the anterior temporal lobe is limited.
b. Lesionectomy: it is indicated in neocortical epilepsy with single well-circumscribed epileptic zone superposed or in proximity to structural lesions; this allows superior surgical results and ES control. The procedure consists of selective resection of an epileptogenic structural lesion, such as certain types of focal cortical dysplasia, cavernomas, circumscribed gliosis, and certain types of developmental tumors such as dysembryoplastic neuroepithelial tumors, gangliogliomas, and some low-grade gliomas. In some cases, the epileptogenic zone may extend beyond the visible lesion, thus requiring an invasive electroencephalogram (EEG) test to locate and determine the extension, as well as to improve the results of the surgery.
c. Neocortical resections: resections of the single or multilobar cortical lesion. This type of surgery requires electrocorticography (intracranial electroencephalography) to establish the extension and the limits of the epileptogenic zone.
d. Functional hemispherectomy: this procedure has substituted the anatomic hemispherectomy due to the risk of residual cerebral hemosiderosis and post-operative hemorrhaging. It consists of total disconnection of the brain hemispheres with limited cerebral tissue resection. It is the indicated procedure for patients with severe hemispheric damage

and refractory motor ES of diverse etiology, whether congenital or postnatal. The causes may be disorders of brain development such as HME, long-term effects of the perinatal vascular event or traumatic brain injury, progressive autoimmune disease such as Rasmussen's encephalitis, Sturge-Weber syndrome, and among others.

e. Callostomy: palliative procedure in which hemispheric disconnection is achieved through the section of the *corpus collosum* in the prevention of interhemispheric seizure propagation and generalization. This procedure is indicated in cases of severe epilepsy with drop attacks.
f. Multiple subpial transections: this procedure is reserved for non-excisable EZ due to their proximity to eloquent areas of the brain cortex. It is frequently associated with cortical resection.
g. Other techniques: stereotactic radiosurgery, VNS, trigeminal nerve stimulation, and DBS[2,20].

What are the minimum tests required for the preoperative evaluation of epilepsy surgery?

Phase 1 of the pre-operative evaluation is the non-invasive portion of the evaluation, and it requires at least:

a. Extensive clinical evaluation with expert review of patient's clinical history and previous laboratory and imaging tests. The identification of associated prognostic factors at the time of seizure onset and throughout the evolution of the disease must be emphasized, as well as seizure semiology during the course of disease, with particular interest in the previous 12 months, including frequency, intensity, duration, aura, and associated trigger factors (emotional stress, sleep-deprivation, menstruation), medications, dosages, combinations, side-effects, memory and language alteration, cognitive deterioration and psychiatric comorbidities. An exhaustive review of previous laboratory and imaging tests, as well as previous hospital records, must be performed whenever possible; for example, finding the activity or epileptic discharge zones in the patient's first EEG will have focalizing or lateralizing value. A large quantity of patients referred to surgical epilepsy centers present pseudoresistance to AEDs. The most common causes include incorrect diagnosis, inadequate pharmaceutical drug selection for the seizure type, inadequate or insufficient dosages, and "irresponsible patient lifestyle choices. Initially, the diagnosis of ES must be corroborated according to international criteria. Subsequently, the diagnosis of RE must be identified and confirmed, ideally based on a thorough review of patient's history and disease evolution.
b. EEG: compatible and consistent serialized EEG and video – EEG (vEEG) monitored by superficial electrodes.
c. MRI: high-resolution cranial MRI that identifies brain anatomy and structural lesions. It is recommended to use resonance equipment in the 1.5-3.0 Tesla range and FLAIR sequences to identify cortical dysplasia. In addition, tractography is recommended to identify Meyer's loop and prevent post-operative quadrantanopsia in temporal lobe surgeries. The Wada test or functional MRI (fMRI) can be performed if the identification of the verbal dominant hemisphere is required.
d. Neuropsychology or developmental evaluation: facilitates the identification of possible lateralization and localization of the epileptogenic zone, as well as determining the pre-operative cognitive status to anticipate possible cognitive surgical side effects.
e. Psychiatric evaluation: necessary to evaluate the patient's comorbidities, as well as the patient's expectations of surgical outcome and quality of life.

In 2006, the sub-commission of pediatric epilepsy surgery of the ILAE concluded that a superficial EEG that includes a record of sleeping cortical electrical activity, an MRI with specific epilepsy protocol and neuropsychological evaluation are required to consider a pediatric patient for epilepsy surgery. A 12-24 h superficial vEEG must record at least one paroxysm, and a brain fMRI must be performed whenever possible[6].

What are the main complications of drug-resistant or RE?

A mortality rate of 2-3 times higher has been recorded for the population with epilepsy. The mortality rate is even more critical in the subgroup of patients with RE, where the standardized mortality rate has been calculated up to 4.69 to 5 times higher than the general population. In addition, within this group of patients, a large proportion of the causes of death are directly related to epilepsy, such as sudden unexpected death. Conversely, when epilepsy surgery is successful in controlling seizures, reduced epilepsy-related mortality risk has been recorded[21].

RE is associated with *non-fatal injuries* such as traumatic brain injury, burns, fractures, work-related accidents, and accidents during recreational and everyday life activities, among others. In addition, RE is

associated to *disabilities and a low quality of life* which can cause a *low academic performance, cognitive decline, and social isolation*. The rate of *employment, matrimony, and fertility* is considerably reduced in patients with poorly controlled ES[2].

The majority of patients with RE has significant restrictions on their everyday life, such as driving motor vehicles. The complications of RE can originate through a combination of effects such as recurrent ES, drug toxicity, and other psychological associated factors such as *depression, anxiety, psychosis,* and excessive *dependence* on a care-taker[9]. In addition to the direct and indirect costs of ES, most patients are referred to surgical evaluation over 20 years after the diagnosis of epilepsy; it is highly likely that this delay in referral is responsible for a significant quantity of deaths related to ES[10]. Finally, the probability of postsurgical seizure remission and favorable quality of life is indirectly related to the time span between RE onset to the moment of epilepsy surgery[10].

Levels of evidence of epilepsy surgery

Data	Levels of evidence
Approximately 17-33% of patients with epilepsy develop RE. (ILAE)	III
Combined surgical and pharmacological treatment are more effective compared to pharmacological treatment alone for temporal lobe epilepsy, and results in greater control of epileptic seizures and improved quality of live	I
Patients with medial temporal lobe RE subjected to early surgery (<2 years) achieve seizure remission more frequently than patients who do not undergo surgery	II
Complete hippocampal resection is more effective than partial resection in patients with medial temporal lobe epilepsy	II
Combined surgical plus rational pharmacological treatment is more effective than pharmacological treatment alone in patients with neocortical epilepsy, a single well-circumscribed lesion and no contraindications of surgery	III
Functional hemispherectomy, or its variants, is safe and efficient surgical techniques for the control of epileptic seizures in patients with hemispheric epilepsy syndromes	III
Multiple subpial transections, with or without resections, reduces the frequency of different types of epileptic seizures	IV
Callostomies can reduce the frequency of drop attack epileptic seizures in a sustained fashion over time	IV
There is no consensus over the quantity of information necessary for pre-operative evaluations, although it must be sequential and staggered, beginning with basic tests and subject to amplification if necessary	IV
The basic information of a pre-operative evaluation includes a detailed clinical evaluation, prolonged record of epileptic seizures through EEG monitor, magnetic resonance imaging with specific epilepsy protocol and neuropsychological/neuropsychiatric evaluations	IV
Video-EEG monitoring with intracranial electrodes is a safe procedure that is associated with minimum permanent morbidity and/or mortality rate	II
The risk of complications is less with deep electrodes compared to subdural sheets	III
When subdural electrodes are used, the risk of complications increases by the number of electrodes	II

References

1. Rathore C, Radhakrishnan K. Concept of epilepsy surgery and presurgical evaluation. Epileptic Disord. 2015;17:19-31.
2. Wiebe S, Blume WT, Girvin JP, Eliasziw M, Effectiveness, efficiency of surgery for temporal lobe epilepsy study group. A randomized, controlled trial of surgery for for temporal-lobe epilepsy. N Engl J Med. 2001; 345(5):311-8.
3. Pindrik J, Hoang N, Smith L, et al. Preoperative evaluation and surgical management of infants and toddlers with drug-resistant epilepsy. Neurosurg Focus. 2018;45:E3.
4. Begley CE, Annegers JF, Lairson DR, Reynolds TF, Hauser WA. Cost of epilepsy in the United States: a model based on incidence and prognosis. Epilepsia. 1994;35:1230-43.
5. 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;51:1069-77.
6. Ryvlin P, Cross JH, Rheims S. Epilepsy surgery in children and adults. Lancet Neurol. 2014;13:1114-26.
7. Andaluza G, Epilepsia D. Diagnóstico y Tratamiento de la Epilepsia en Niños y Adultos. Sociedad Andaluza de Epilepsia. Viguera Editores. Saint Louis: Saint Louis University; 2015.
8. Helmstaedter C. Neuropsychological aspects of epilepsy surgery. Epilepsy Behav. 2004;5 Suppl 1:S45-55.
9. Helmstaedter C. Cognitive outcomes of different surgical approaches in temporal lobe epilepsy. Epileptic Disord. 2013;15:221-39.
10. Engel J Jr., 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;60:538-47.
11. Téllez-Zenteno JF, Dhar R, Wiebe S. Long-term seizure outcomes following epilepsy surgery: a systematic review and meta-analysis. Brain. 2005;128:1188-98.
12. West S, Nolan SJ, Cotton J, et al. Surgery for epilepsy. Cochrane Database Syst Rev. 2015;7:CD010541.
13. Sander JW, Shorvon SD. Epidemiology of the epilepsies. J Neurol Neurosurg Psychiatry. 1996;61:433-43.
14. Kalilani L, Sun X, Pelgrims B, Noack-Rink M, Villanueva V. The epidemiology of drug-resistant epilepsy: a systematic review and meta-analysis. Epilepsia. 2018;59:2179-93.
15. Pre-surgical evaluation for epilepsy surgery European standards. European federation of neurological societies task force. Eur J Neurol. 2000; 7:119-22.
16. Engel J Jr. Mesial temporal lobe epilepsy: what have we learned? Neuroscientist. 2001;7:340-52.
17. Semah F, Picot MC, Adam C, et al. Is the underlying cause of epilepsy a major prognostic factor for recurrence? Neurology. 1998;51:1256-62.
18. Jayakar P, Gaillard WD, Tripathi M, et al. Diagnostic test utilization in evaluation for resective epilepsy surgery in children. Epilepsia. 2014; 55:507-18.
19. Wyllie E, Comair YG, Kotagal P, et al. Seizure outcome after epilepsy surgery in children and adolescents. Ann Neurol. 1998;44:740-8.
20. Engel J Jr., McDermott MP, Wiebe S, et al. Early surgical therapy for drug-resistant temporal lobe epilepsy: a randomized trial. JAMA. 2012; 307:922-30.
21. Ryvlin P, Kahane P. Does epilepsy surgery lower the mortality of drug-resistant epilepsy? Epilepsy Res. 2003;56:105-20.