

โครงการ ศูนย์ความเป็นเลิศโรคลมชักรามาธิบดี (Rama Epilepsy Excellent Center)

How to select good surgical candidate?

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Epilepsy surgery

- Epilepsy surgery has been shown to be an effective treatment for patients with drug-resistant epilepsy.*
- Identification of the appropriate epilepsy surgical candidate is a fundamentally important aspect of epilepsy care.

Early Surgical Therapy for Drug-Resistant Temporal Lobe Epilepsy A Randomized Trial

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Design, Setting, and Participants The Early Randomized Surgical Epilepsy Trial (ERSET) is a multicenter, controlled, parallel-group clinical trial performed at 16 US epilepsy surgery centers. The 38 participants (18 men and 20 women; aged \geq 12 years) had mesial temporal lobe epilepsy (MTLE) and disabling seizues for no more than 2 consecutive years following adequate trials of 2 brand-name AEDs. Eligibility for anteromesial temporal resection (AMTR) was based on a standardized presurgical evaluation protocol. Participants were randomized to continued AED treatment or AMTR 2003-2007, and observed for 2 years. Planned enrollment was 200, but the trial was halted prematurely due to slow accrual.

Intervention Receipt of continued AED treatment (n=23) or a standardized AMTR plus AED treatment (n=15). In the medical group, 7 participants underwent AMTR prior to the end of follow-up and 1 participant in the surgical group never received surgery.

Main Outcome Measures The primary outcome variable was freedom from disabling seizures during year 2 of follow-up. Secondary outcome variables were healthrelated QOL (measured primarily by the 2-year change in the Quality of Life in Epilepsy 89 [QOLIE-89] overall T-score), cognitive function, and social adaptation.

Results Zero of 23 participants in the medical group and 11 of 15 in the surgical group were seizure free during year 2 of follow-up (odds ratio = ∞ ; 95% CI, 11.8 to ∞ ; P < .001). In an intention-to-treat analysis, the mean improvement in QOLIE-89 overall T-score was higher in the surgical group than in the medical group but this difference was not statistically significant (12.6 vs 4.0 points; treatment effect=8.5; 95% CI, -1.0 to 18.1; P=.08). When data obtained after surgery from participants in the medical group were excluded, the effect of surgery on QOL was significant (12.8 vs 2.8 points; treatment effect=9.9; 95% CI, 2.2 to 17.7; P=.01). Memory decline (assessed using the Rey Auditory Verbal Learning Test) occurred in 4 participants (36%) after surgery, consistent with rates seen in the literature; but the sample was too small to permit definitive conclusions about treatment group differences in cognitive outcomes. Adverse events included a transient neurologic deficit attributed to a magnetic resonance imaging–identified postoperative stroke in a participant who had surgery and 3 cases of status epilepticus in the medical group.

Conclusions Among patients with newly intractable disabling MTLE, resective surgery plus AED treatment resulted in a lower probability of seizures during year 2 of follow-up than continued AED treatment alone. Given the premature termination of the trial, the results should be interpreted with appropriate caution.

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JAMA. 2012;307(9):922-930.

Complications of drug-resistant epilepsy

- Impaired quality of life
- Epilepsy-related disabilities
 - poor academic performance
 - unemployment
 - psychosocial problems
 - cognitive and behavioral dysfunction
 - seizure-related injury
- Increased morbidity
- Increased mortality



Treatment of epilepsy

• The management of patients with epilepsy is focused on three main goals:

1. No seizures of any type (seizure freedom)

- 2. No adverse effects from anti-seizure medication, and/or treatment
- 3. Normal quality of life

Cost-effective screening

- How to select good surgical candidates?
 - Who is a good surgical candidate?
 - When the patient should be referred to the epilepsy center?

Clinical evaluation

- History taking
- Seizure semiology?
 - from the patient
 - from the witness
 - any lateralizing signs
- How many seizure types?
 - seizure type 1
 - seizure type 2

Review

Lateralizing signs during seizures in focal epilepsy

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Clinical evaluation

- Review of past and current medications
- Impacts of seizure on quality of life
- Past medical history
- Psychosocial issues
- Behavioral problems

Appropriate management in each patient

- Medical treatment
- Surgical treatment (palliative vs curative epilepsy surgery)
 - establish drug-resistant epilepsy
 - rule out pseudo- resistance
 - any contraindications for epilepsy surgery

Basic concept of epilepsy surgery

Definition of abnormal brain areas

	Definition	Measures
Epileptogenic zone	The area of brain that is necessary and sufficient for initiating seizures and whose removal or disconnection is necessary for abolition of seizures	Theoretical concept
Irritative zone	Area of cortex that generates interictal EEG	EEG
Ictal onset zone	Area of cortex where seizures are generated	EEG
Epileptogenic lesion	Structural abnormality of the brain that is the direct cause of the epileptic seizures	Neuroimaging, tissue pathology
Symptomatogenic zone	Portion of the brain that produces the initial clinical symptomatology	Behavioral observation and patient report
Functional deficit zone	Cortical area of non-epileptic dysfunction	Neurologic exam, neuropsychological testing, EEG, PET, SPECT

Epilepsy surgery

- The accurate localization and delineation of the extent of the epileptogenic zone
- Complete resection of the epileptogenic zone
- Postoperative seizure freedom

Selection of ideal candidates for epilepsy surgery

- Drug-resistant epilepsy *
- Seizures causing significant disability and impaired quality of life
- Epileptogenic zone can be localized.
- Acceptable risks and benefits of epilepsy surgery

Indications for epilepsy surgery

- Drug-resistant epilepsy *
- Focal epileptogenic structural lesion
- Single epileptogenic focus amendable to resection
- Surgically remediable syndrome **

*Epilepsia. 2010 Jun;51(6):1069-77

Relative contraindications for epilepsy surgery

- Progressive medical or neurological disorder
- Primary generalized epilepsy
- Minor seizures which do not impaired the quality of life.
- Active psychosis that is not related to peri-ictal period.
- Poor contralateral memory function (for temporal lobectomy)

Case #1: Focal epileptogenic structural lesion

- A 38 yo right handed male with drug-resistant temporal lobe epilepsy who is here for seizure evaluation. The history of seizure began at the age of 18.
 - seizure type 1: complex partial seizure seizure frequency: 2-3 times per month lateralizing signs: postictal nose wiping
 - PHT +CBZ
 - EEG: epileptiform discharge at right temporal
 - brain MRI: cavernoma right parieto-occipital lobe

Case#1: Right parietal craniotomy with cavernoma excision and electrocorticography (ECoG) 03/16/2015





ECoG showed few spikes at antero-inferior side of the lesion



No seizure since March 2015

Normal quality of life since then

Surgically remediable epilepsy syndromes

- Characteristic features:
 - known pathophysiology
 - predictable natural history
 - unresponsive to pharmacotherapy
 - progressive features (e.g., developmental delay, psychosocial disturbances)
- Epilepsy surgery is the most effective method.
 - 70-90% chance of seizure free

Surgically remediable epilepsy syndromes

- Mesial temporal lobe epilepsy
- Epilepsies due to well-circumscribed resectable lesions
- Epilepsies in infants and young children due to large or diffuse lesions limited to one hemisphere (e.g., porencephalic cysts, Rasmussen's encephalitis, Sturge-Weber syndrome, hemimegalencephaly, and other large malformations of cortical development)

When the patient should be referred for presurgical evaluation?

When the patient should be referred to an epilepsy center?

- Currently, there is no standard referral criteria.
- Operational definition of drug-resistant epilepsy by ILAE*
- RAND/UCLA Appropriateness Method**

*Epilepsia. 2010 Jun;51(6):1069-77

**Seizure. 2012 Jan;21(1):32-9.

Development of an electronic decision tool to support appropriate treatment choice in adult patients with epilepsy--Epi-Scope(®).



Conceptual model of the panel study. Treatment recommendations for adult (16+) patients with

epilepsy were formulated based on the appropriateness of

antiepileptic drugs (AEDs) with respect to particular clinical variables

Definition of drug resistant epilepsy: Consensus proposal by the ad hoc Task Force of the ILAE Commission on Therapeutic Strategies

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• "Failure of adequate trials of two tolerated and appropriately chosen and used AED regimens whether as monotherapy or in combination to achieve sustained <u>seizure freedom</u>"

Evaluation of duration of epilepsy prior to temporal lobe epilepsy surgery during the past two decades

Hyunmi Choi^{a,*}, Richard Carlino^a, Gary Heiman^c, W. Allen Hauser^{a,b}, Frank G. Gilliam^d

		Cure a h	Cura in D	6	
Table 2	Mean values (SD) for duration of	epilepsy prior t	o temporal lobe epilepsy sur	gery according to year of	surgery.

	Group A	Group B	Group C	p-Value
Mean duration in years (SD)	22.6 (12.7)	22.4 (15.4)	21.1 (14.2)	0.54 ^a
^a ANOVA.				

The mean duration of epilepsy prior to temporal lobe epilepsy is 20 years.

Ramathibodi hospital(late 2014-2015)

Drug-resistant epilepsy cases	Time from first seizure to comprehensive evaluation (years)
1	б
2	12
3	15
4	21
5	26
6	33
7	36

Five of them are potential good surgical candidates.

Long delay in pre-surgical evaluation

- The reasons are not completely understood.
- The possible explanations are as follows.
 - self-reported seizure rates
 - afraid of having a brain surgery
 - a remitting-relapsing course of epilepsy
 - does not follow the available standard guideline
 - lack of timely referral to epilepsy surgery centers by the treating neurologists or primary care physicians

Clinical patterns of drug-resistant epilepsy

- 1. Refractory de novo
- 2. Delayed refractoriness
- 3. Wax-and-wane pattern
- 4. Delayed responsiveness



Different clinical patterns of drug resistance. De novo continuous drug resistance (—), reversal of drug resistance, possibly in a intermittent pattern in which periods of remission are followed by periods of uncontrolled seizures (- -), and progression to drug resistance of delayed onset with persistent loss of efficacy after initial control (--). See text for description of clinical patterns and discussion of putative mechanisms.

Common misconceptions about who should be referred for surgical evaluation

Clinical

- elderly
- memory deficits
- low IQ (<70)
- psychiatric disorders

Anti-seizure medications

- All anti-seizure medications need to be tried.

Common misconceptions about who should be referred for surgical evaluation

Electroencephalography (EEG)

- bilateral interictal epileptiform discharges

Case #2: 34 yo female with drug-resistant temporal lobe epilepsy

- on 3 anti-seizure medications

- MRI: cystic encephalomalacic changes at right anterior temporal lobe
- EEG: interictal on both sides(left 70%, right 30%)
- VEEG: EEG seizure onset on right hemisphere







Common misconceptions about who should be referred for surgical evaluation

Neuroimaging

- normal brain MRI
- multiple or diffuse lesions on MRI
- lesions on the dominant cerebral hemisphere

Case#3: normal brain MRI

• A 46 yo female presents with drug-resistant epilepsia partialis continua for one day.



left temporal arachnoid cyst



Todd's paralysis

Case#3: normal brain MRI: invasive EEG monitoring + intraoperative electrocorticography (ECoG) showed spikes at left parietal lobe.+ cortical mapping on July 2014





Conclusions

- The treatment goals in epilepsy
 - No seizures of any type (seizure freedom)
 No adverse effects from anti-seizure medication
 Normal quality of life

• Patients with drug-resistant epilepsy who have tried at least two different antiepileptic medications, but still suffer from seizures and/or disabling side effects from anti-seizure medications that affect their quality of life. These patients should be referred to the epilepsy center for comprehensive epilepsy evaluation.

Thank you