



## A screening tool to identify surgical candidates with drug refractory epilepsy in a resource limited settings



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### ABSTRACT

**Objectives:** Access to epilepsy surgery remains a considerable challenge in contemporary healthcare systems. Given the limitations in resources and demand for Epilepsy Monitoring Unit (EMU) assessments, information that can be used to expedite the process is of great value. The purpose of this study was to identify variables prior to EMU admission that may be associated with candidacy for prospective epilepsy surgery.

**Methods:** This was a prospective study conducted at the Department of Neurology, All India Institute of Medical Sciences, New Delhi, India. We identified two subgroups of patients from 501 drug refractory epilepsy (DRE) patients admitted in EMU of Neurology Department, AIIMS from 2006 onwards following validation of proposed tool in 40 patients. They on subsequent investigations were either cleared or not cleared for epilepsy surgery. A tool consisting of variables likely to predict surgical candidacy in persons with DRE in Indian settings was developed for identification of patients who might benefit from an early epilepsy surgery evaluation.

**Results:** Statistical analysis revealed significant differences between the two groups for several variables. Non-surgical candidates had non-disabling seizures, seizures improved with a combination of drugs, had little/no AEDs side effects and had near normal or normal scalp EEG and MRI brain.

**Significance:** Using the best available evidence, we developed a decision making tool which can provide a comprehensive quick guide for determining candidacy for epilepsy surgery evaluations in resource limited settings. Given the demand for EMU assessments, information that can be used to expedite the process is of value.

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## 1. Introduction

Epilepsy is a common chronic disorder with episodic manifestations. Nearly 1% of the world's population is affected by this debilitating neurologic disorder (Devinsky, 2004).

Most of the health care costs of epilepsy are due to drug refractory epilepsy (DRE) (Begley et al., 1994). Misguided and perceived stigma (Sujoy et al., 2005) and years of uncontrolled epilepsy can lead to cognitive decline (Thompson and Duncan, 2005), poor quality of life (QOL) (Spencer et al., 2007), increased mortality (Sperling et al., 1999) and high societal costs through loss of productivity and medical care expenditures (Jacoby et al., 1998). In some health

care systems, epilepsy surgery is less costly than ongoing medical therapy, with health care costs declining substantially after successful surgery (Langfitt et al., 2007). Best practice dictates that patients who are treatment resistant (failure of adequate trials of 2 antiseizure medications) should undergo extensive epilepsy evaluation including epilepsy surgery (Kwan et al., 2010). Admission to the Epilepsy Monitoring Unit (EMU) is the essential diagnostic protocol in specialized epilepsy centers where care is provided by a collaborative multidisciplinary team supervised by a neurologist or neurosurgeon with expertise in epilepsy (Labiner et al., 2010).

Currently, on an average, patients who do get surgery have had DRE for two decades or more. Many who come for evaluation had never known that they might be candidates for epilepsy surgery. Causes of this treatment gap are complex, but “knowledge gap” and a “feasibility gap” are two most important factors responsible (Jehi and Mathern, 2015).

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Lin et al., in 2010, conducted a retrospective review for the clinical data of 112 non-surgical candidates after presurgical evaluation for epilepsy surgery. The common causes of non-surgical decisions after presurgical evaluation were patients and their families giving up intracranial electrode placement for various reasons (37.5%), multifocal epileptogenic zones (25.9%), generalized seizures (13.4%), pseudo-seizure or slight seizure (8.9%), epileptogenic zones in functional areas (5.4%) and so on (Lin et al., 2010).

Alireza et al., in 2013, carried out a retrospective analysis of 414 patients admitted for pre-surgical evaluation. Overall, 259 patients (62.5%) were identified as potential surgical candidates. Male patients and those with a lesion on MRI were 1.9 times more likely to be surgical candidates. In this study male gender, presence of a lesion on MRI and localizable seizures on routine outpatient EEG analysis independently predicted subsequent resective epilepsy surgical candidacy in EMU patients (Mansouri et al., 2013).

Although excellent epilepsy surgery related guidelines have been published over the years, guideline implementation is typically poor. We in India too have guidelines (Chandra and Tripathi, 2010) to reduce the epilepsy surgery treatment gap and to ensure timely referral for evaluation, a new approach is needed to assist physicians in identifying patients who might benefit from an extensive epilepsy surgery evaluation as surgery offers a possibility of good outcomes (Chandra et al., 2014).

Given the limitations in resources and demand for EMU assessments, information that can be used to expedite the process is of great value. Here, we sought to identify variables prior to EMU admission that may be associated with candidacy for respective epilepsy surgery.

## 2. Methods

This was a prospective study conducted at the Department of Neurology, All India Institute of Medical Sciences, New Delhi, India (from 2006 to 2014).

The patients were recruited from the EMU. All patients admitted to the EMU had DRE. They all were not responding to two or more AEDs, over several years. They had have taken medications with regular compliance and adequate dose. In all pseudoseizures were ruled out based on an outpatient VEEG (3 h) with induction. Diagnosis of seizures was made on the basis of history as well as clinical examination. MRIs were done on 3.0T Scan with a pre-specified Epilepsy protocol.

Patient's personal and demographic details along with the complete description of seizures and investigations were recorded. Various parameters were assessed in both groups (Cleared for surgery and Not cleared for surgery) as per Web-based clinical decision tool, the Canadian Appropriateness of Epilepsy surgery (CASES) tool ([www.epilepsycases.com](http://www.epilepsycases.com)) developed using the RAND–UCLA appropriateness methodology after taking due permission (Appendix 1). Ethical clearance was obtained from the ethics committee of the institute before the commencement of the study. It consisted of variables like number of adequate AEDs trials, seizure severity, AEDs side effects, seizure frequency, epilepsy duration, seizure type, investigations like EEG and MRI. In addition, individual factors like gender, age of onset of seizures, perinatal insult too were assessed in all the enrolled patients. Taking into account RAND–UCLA appropriateness methodology and additional variables likely to predict surgical candidacy in persons with DRE in our Indian settings based on our experience, we developed a tool consisting of following variables for early identification of patients who might benefit from an epilepsy surgery evaluation.

Presurgical Evaluation Tool for Refractory Epilepsy (PETRE)

Variable	Categories
Age of onset of seizures	1. <12 years 2. >12 years.
Gender	1. Male 2. Female
History of perinatal insult	1. Present 2. Absent
Seizure type	1. Simple partial seizures 2. Complex partial seizures/GTCS 3. Drop attacks/tonic seizures/myoclonus 4. Multiple seizures types
Seizure duration	1. <1 year 2. >1 year
Seizure severity	1. Disabling seizures <sup>a</sup> 2. Nondisabling seizures
Number of adequate AEDs tried	1. 1 2. 2 3. 3 4. More than or equal to 4
AEDs side effects	1. Yes 2. No
Seizure frequency	1. Seizure free 2. <1 seizure/year 3. Less than 1 seizure/month 4. More than 1 seizure/month
<i>Investigations</i>	
Interictal pre EMU EEG	1. Normal 2. Abnormal
MRI	1. Normal 2. Abnormal
If MRI abnormal	1. Multifocal or bilateral involvement <sup>b</sup> 2. Unifocal involvement

<sup>a</sup> Disabling seizures:- seizures causing impairments, activity limitations, and participation restrictions (WHO definition of disability).

<sup>b</sup> Especially perinatal insult sequale bilateral MRI findings were assessed in view of high prevalence in our settings.

The tool consisted of 12 points and was filled after a detailed history taking and investigations. The tool language was English. Tool try out was done in 40 subjects, prior to use and was found to be appropriate for the DRE population being studied. Time taken to fill out the tool was 20–30 min.

The proposed tool, presurgical evaluation tool for refractory epilepsy (PETRE), was filled for all the DRE patients admitted in our EMU who were enrolled in the study. After assessment and discussion in the multidisciplinary epilepsy surgery meet (ESM), patients were divided in two subgroups viz. cleared and not cleared for epilepsy surgery. ESM consisted of discussions pertaining to the assessment of clinical history of patient, seizure semiology, interictal EEG and VEEG recordings of the patient from Neurology department, 3T epilepsy protocol MRI assessment by the Neuroradiology department and PET, SPECT (ictal and interictal), SISCOS review from the Nuclear Medicine department of our institute. In case of mesial temporal lobe epilepsy (MTLE), at least three events were recorded and in cases of extratemporal lobe epilepsy (ETLE), about 5–11 (more recorded in case of discordant or bilateral ictal onsets) events were recorded. VEEG assessment consisted of detailed evaluation of seizure semiology and ictal onsets. If this was not concordant with the MRI findings or when MRI was normal, then further noninvasive evaluations like SPECT, PET or MEG were done. Based upon detailed discussions and evaluation of all these parameters, the patient was cleared or not cleared for surgery by the ESM team. These two groups were then further compared with respect to each variable in the tool to see for differences in various variables.

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