Surgery for Drug-resistant Focal Epilepsy

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Epilepsy is a common and a complex neurological disorder that affects health and quality of life. It has been estimated that there are 10 million people with epilepsy (PWE) in India. These PWE have an increased risk of seizure-related death and disability. Effective treatments are available for many types of epilepsy, but timely referrals and access to these treatments fall short. Currently, forty different types of antiepileptic drugs (AED) are available. However, all these drugs together can control seizures in only 60%–70% of PWE. The remaining, 30-40% of PEW continues to have seizures in spite y of AED and constitute the drug resistant epilepsy (DRE) group.¹

Now we have class 1 evidence² that epilepsy surgery is significantly more efficacious than continued medical treatment in people with DRE. However, epilepsy surgery is highly underutilized or overly delayed in India. There are several reasons underlying the delay in the referral. National Institutions in India like ScTI MST at Trivandrum,³ AIIMS at New Delhi and NIMHANS at Bangalore and other centers have successfully established cost-effective epilepsy surgery programmes (ESP) over the past two decades. However, considering the magnitude of the patients who are likely to be benefited by epilepsy surgery, several centers which can cater to the needs of these PWE, require to be developed in India in the near future.⁴ During this brief write-up, I will summarize the current status of epilepsy surgery and outline the pre-requisites to establish ESP successfully.

Pre-surgical Evaluation

People with DRE have to undergo detailed presurgical evaluation to find out the surgery candidacy and the expected outcome. The standard pre-surgical evaluation includes careful analysis of history and clinical features, non-invasive tests consisting of high resolution epilepsy protocol based on cerebral MR imaging, scalp video-EEG telemetry and neuropsychological assessment. Concordance of data obtained from these tests may be adequate to perform surgery with good results, as in the classical mesial temporal epilepsy syndrome (MTLE) with mesial temporal sclerosis (MTS) or circumscribed and discrete neocortical lesions such as dysembryoplastic tumours, low-grade astrocytomas, focal vascular abnormalities and malformations of cortical development like focal cortical dysplasia.

Neuroimaging

In recent years, tremendous advances in the neuroimaging have had a profound effect on the pre-surgical evaluation and surgical management of people with DRE. High resolution magnetic resonance imaging (MRI) is now capable of identifying the structural pathology underlying DRE in most patients. In clinical situations, where MRI brain is either normal, equivocal, demonstrate multiple lesions or lesion is adjacent to the eloquent cortex, then epileptogenic zone can be reliably predicted by careful correlation of clinical, EEG and functional imaging findings. Functional imaging techniques such as single-photon emission computed tomography (SPECT) or positron emission tomography (PET) may give localizing information about ictal cerebral blood flow, glucose metabolism, or benzodiazepine (BZD) receptors that implicate a more widespread physiologic abnormality.

Clinical Electrophysiology

Electroencephalography (EEG) is the most important test in epileptology. During the past several decades, considerable effort has been devoted to the development of several electrophysiological techniques in pre-surgical evaluation namely visual analysis of inter-ictal and ictal EEG findings obtained during routine scalp and intracranial recording; stereo-EEG and magnetoencephalography (MEG) among others.

Surgical Procedures

Epilepsy surgery is the resection or functional manipulation of part of the brain with the aim of alleviating seizures, improving the cognitive function and the quality of life. The principle of epilepsy surgery is to identify and resect or disconnect a single identifiable epileptogenic focus and or lesion without risk of neurological deficit. It has been reported that the success of epilepsy surgery depends upon the accurate localization of the epileptogenic zone, which is defined as the area necessary and sufficient for initiating seizures and whose removal or disconnection is necessary for abolition of seizures.

Surgery for Temporal Lobe Epilepsy

MTLE with MTS is most common cause of DRE and anterior temporal lobectomy along with amygdalohippocampectomy is the most common epilepsy surgery procedure. Surgery for MTLE with MTS leads to improvement in seizure control, cognitive function and quality of life. Suitable surgical candidates for ATL can be identified with standardized non-invasive protocols and the outcome will be cost effective. There are a number of surgical techniques, including the standard ATL, tailored ATL and selective amygdalohippocampectomy with different variations. However, it is preferable to perform standard ATL in the majority of cases with modifications based upon cerebral dominance, cortical vasculature and neuropsychological status. We have to take measures to optimize the seizure outcome as well as avoidance of surgical, neurological and neuropsychological deficits.

Surgery for Extra-Temporal Epilepsy

In contrast to temporal lobe surgery, extra-temporal epilepsy surgery demands complex pre-surgical evaluation and innovative surgical approaches. Outcome in extra temporal epilepsy surgery was reported to be inferior to temporal lobe surgery. However, recent data suggests that resection of discrete small epileptogenic lesions in the extra temporal regions also leads to good outcome. Frontal lobe epilepsy surgery prevails in this category. Non-lesional extra temporal epilepsy surgery usually requires extensive invasive pre-surgical evaluation, which differs from patient to patient according to the non-invasive findings. Invasive EEG with grid-, strip- and depth-electrodes, often in combination, is necessary, to delineate the epileptogenic seizure onset zone. In non-lesional extra temporal epilepsies circumscribed corticectomies are rarely successful.

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more often rather extensive resections are required to render a patient seizure-free. Incomplete resection can be due to poor differentiation of lesion from the normal brain or the extension of the structural abnormalities to a functional area.

Lesional Epilepsy Surgery

Lesionectomy for epilepsy is a surgical procedure that is directed at the structural lesion, believed to be the etiology of the seizure disorder. It has been reported that, in the case of isolated structural lesions such as dysembryoplastic tumours, low-grade astrocytomas, focal vascular abnormalities, total macroscopic and radiologic evidence of lesonal excision is associated with excellent seizure-free outcome. The extent of the resection may be determined by different criteria: (1) intra-operative visualization of the tissue; (2) radiological margins determined by MRI signal abnormalities; (3) histologic margins based on intra-operative frozen section evaluation of the tissue; (4) electrocorticographic margins based on intra-operative ECoG; and (5) intra-operative MRI or ultrasound evaluation or a combination of these techniques.

Pediatric Epilepsy Surgery

In the pediatric patients, diagnosis of DRE should be made much earlier, particularly if children present with epileptic encephalopathy, infantile spasms, catastrophic onset of epilepsy, frequent and disabling seizures. Children with specific epilepsy syndromes such as: Sturge–Weber syndrome, hemispheric syndromes, Rasmussen’s encephalitis and hypothalamic hamartoma should be referred for pre-surgical evaluation without delay and if found suitable, surgery should be offered earlier. In children presenting with drug-resistant and disabling seizures without delineation of an epileptogenic zone or Lenox Gestalt syndrome, functional procedures such as corpus callosotomy can be performed especially to control the drop attacks.

Stereotactic Techniques

Stereotactic techniques have been used in India for both temporal lobe epilepsy as well as generalized seizures. However, since the introduction of image guidance, these techniques are being used currently for the electrode implantation of both depth and subdural electrodes, as well as to localize lesions and facilitate anatomic resections. Stereotactic laser ablation of the hippocampus under MR thermal imaging is an emerging technique.

Radiosurgery

Radiosurgery (RS) for management of DRE has been introduced in the past two decades. Radiosurgery is being proposed in cases of refractory seizure wherein the epileptogenic focus can be well defined radiologically and is smaller in volume. The classical conditions which are being considered are mesial temporal sclerosis, hypothalamic hamartoma and arteriovenous malformations. The outcome of RS has been reported to be at par with surgery. However, the long term neurobiological effects of RS are yet to be identified.

Neurostimulation

Electrical stimulation to treat seizures in patients who are not suitable for resective surgery is a novel idea. Electrical stimulation is reversible. If it does not work, it can be discontinued and the electrodes can be removed. Neuronal tissue needs not be destroyed or resected, except for the tissue directly along the tract of the stimulating electrodes. Stimulation can occur within seconds, enabling patients to turn the stimulator on at the beginning of a seizure.

Vagal Nerve Stimulation

Though the exact mechanism by which the vagal nerve stimulation controls seizure is still unknown, it was felt that continual stimulation of the vagus nerve by an implantable electrical device might result in wide-spread bilateral activation or de-activation of the brain circuits thought to be involved with epileptic seizures. The efficacy of the vagal nerve stimulation is based on two randomized control trials which reported a modest response of reduced frequency of seizures by 50% or more in 30–40% of patients. This technique is currently being proposed in select cases of non-localized drug resistant epilepsy, where resective surgery is not the option. In comparison to the corpus callosotomy, VNS is expensive, but reversible procedure.

Deep Brain Stimulation in Epilepsy

There are indications that deep brain stimulation (DBS) improves seizure control in a group of patients previously not suitable for resective surgery. Stimulation of the centrum medianum and the anterior nuclei of the thalamus, subthalamic nucleus, as well as amygdalo-hippocampal complex have been performed with partial seizure control. Responsive stimulation (RNS), cortical and hippocampal stimulations are other alternatives.

Need to Establish New Epilepsy Surgery Centers

The International League against Epilepsy (ILAE) working group in surgery suggested a two-tiered structure for the surgical management of epilepsy, with a basic center providing a service to adults with more straightforward surgically remediable epilepsy and an academic reference center offering facilities for invasive recording and the treatment of children and basic scientific and clinical research.

Basic Epilepsy Surgery Centers

Basic epilepsy surgery units can be developed in all the medical college hospitals in India which cater to a sizable number of people with epilepsy and where the infrastructure and capability to identify people with DRE exists. Among the people with DRE, in order to identify candidates with surgically remediable epilepsy syndromes, the essential requirements are video EEG telemetry and MRI. Since more and more surgically remediable epilepsy syndromes that do not need expensive and invasive pre-surgical work have been identified, these patients can be operated in these new epilepsy centers. These new centers can cater to people with DRE with MTLE and MTS and other circumscribed structural lesions. They should be able to identify ideal surgical candidates for anterior temporal lobectomy where pre-surgical evaluation will be simple through a standardized non-invasive protocol and the surgical outcome will be good. The difficult cases can be referred to the established centers. It is essential to know which patients may benefit from surgery with the limited facilities and which patients will need further studies. This step-wise approach by reserving more difficult to treat patients to a later date as experience develops, or by referring them to a better-equipped center, will help the basic
surgery units to establish very well in India. These units also need to work with and educate the local public and professionals, if their epilepsy surgery programmes were to have a lasting impact.

**Referral Centres**

In contrast to the basic surgical units, the referral units should have full-fledged facilities for the evaluation and management of people with DRE. In addition to video EEG telemetry and MRI, these centres can have functional imaging such as fMRI, PET and SPECT studies as well as capability for invasive evaluation. These units should be able to perform temporal as well as extra-temporal, multi-lobar and hemispheric resections and functional procedures like corpus callosotomy, multiple subpial transections, neuro-stimulation and radiosurgery.

**Conclusions**

In India, national institutions have successfully established comprehensive epilepsy care programmes and proved that surgery for epilepsy is not only feasible, but can be done in a cost effective way. With the establishment of a number of new basic epilepsy surgery units as well as referral centers, a sizable number of people with drug resistant focal epilepsy can now undergo pre-surgical evaluation and surgical management. Physicians could play a major role in reducing the population of people disabled by epilepsy in India by proper identification and timely referral to a comprehensive epilepsy care programme.

**References**