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SURGERY OF REFRACTORY TEMPORAL LOBE EPILEPSY – THE ONLY TREATMENT MODALITY?

INTRODUCTION

Mesial temporal lobe epilepsy (MTLE) is the most common pharmacoresistant epilepsy in adults, and hippocampal sclerosis (HS) is the most common substrate responsible for epileptogenesis among these patients. [1] A relatively restricted epileptogenic zone and frequent intractability makes MTLE/HS the most surgically amendable epileptic syndrome.[2]

These include Spencer type anteromesial temporal lobectomy (AMTR) with more extensive mesial resection and limited ablation of the temporal neocortex and several variants of amygdalohippocampectomy (AHE).[3,4,5] These procedures have been shown to produce long-term cure rates of approximately 60%–80%.[6]

Most authors have found that patients with complete resections of the mesial temporal structures (hippocampus, parahippocampal gyrus [PHG], and, possibly, the amygdala) have the best chance of seizure-free outcomes. [7]

The search for surgical techniques which may obviate these complications is therefore justifiable. Ideally, these techniques should 1) eliminate unnecessary cortical and white matter tract trauma, 2) avoid manipulation of the cerebral vessels and cranial nerves, 3) attack as little of the mesial temporal structures as is necessary for seizure relief while leaving a maximum of potentially functional tissue undisturbed, and 4) be a relatively simple and safe procedure with a short hospital stay.

METHODS

Anterior temporal lobectomy

Temporal lobectomy is the definitive treatment for medically intractable temporal lobe epilepsy. When seizures are not controlled by 2 different AED trials, the pa-

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tient should be considered for a presurgical evaluation. These patients are not likely to achieve seizure control with medications alone (5–10% chance of becoming seizure free).

The presence of unilateral hippocampal sclerosis and concordant EEG findings predict seizure-free outcome in patients considered for surgery.

Foldvary and colleagues showed that a higher monthly preoperative seizure frequency is associated with a less favorable surgical outcome. [8]

An extensive presurgical assessment for the feasibility of surgery is essential. This includes MRI, interictal and ictal EEG, neuropsychological testing, and the intracarotid amobarbital test called the Wada test.

Seizure-free state at 2 years postoperatively is predictive of long-term seizure-free outcome. In well-selected cases, 70–80% of patients with refractory temporal lobe epilepsy become seizure free after surgery.

Selective amygdalohippocampectomy

Selective amygdalohippocampectomy (SAH) is a more targeted mesial temporal resection that spares the temporal neocortex. Bandt et al examined seizure response rates, complications, and neuropsychological outcomes of trans-middle temporal gyrus SAH for medically intractable mesial temporal lobe epilepsy in 76 adult patients, 19 of whom underwent preoperative and postoperative neuropsychological evaluations. [9]

In this study, favorable seizure response rates were achieved in 92% of the patients, and rates of surgical morbidity were low.[9] Whereas a decline in verbal memory was observed in the left SAH group, improvements in memory were seen in the right SAH group.

Vagus nerve stimulation

In VNS, a battery-operated stimulator device is implanted in the chest and an electrode is attached to the left vagus nerve in the neck. As previously mentioned, vagus nerve stimulation (VNS) was approved by the FDA in 1997 for the treatment of intractable partial epilepsy in patients aged 12 years and older.

VNS with a high-frequency stimulation rate has been found to result in a mean reduction in seizure frequency of 25–28% at 3 months but with improvement to about 40% by year 1. The exact mechanism through which VNS exerts its antiepileptic effect is not known.

Adverse effects of VNS treatment include hoarseness of voice, cough, local pain, paresthesias, dysphagia, and dyspnea when the device is on and almost none when the device is off, but the settings can be titrated so that side effects are minimized. VNS does not have the adverse effects associated with AEDs and is used adjunctively with AEDs.

Stereotactic amygdalohippocampotomy

Stereotactic epilepsy surgery has a long history. Originally, these procedures (fornicotomy and anterior commissurotomy) focused on the improvement of behavioral disorders in epileptic patients and the prevention of seizure spread. [10] It was subsequently noted that stereotactic amygdalotomy reduced seizure frequency in certain patients. A 50% reduction of seizure frequency was reported after stereotactic lesions in the amygdala and hippocampus, but the seizure-free rate was low (10%).[11] Amygdalohippocampal stereotactic lesions using a trajectory passing through the long axis of hippocampus were first created by brachytherapy.[12]

Stereotactic AH is a promising method in the treatment of intractable patients with MTLE. The results suggest that SAH could be superior to open surgery in terms of its neurocognitive outcomes. SAH could be an alternative therapy for MTLE.[13] Further randomized prospective multicenter studies are warranted to prove this concept.

Stereotactic Radiosurgery

The first attempts at radiosurgical interventions indicated for primarily epileptologic reasons were performed by fractionated radiotherapy using a linear accelerator and irradiation by a cobalt irradiator with positive epileptologic results reported [14,15]. The excellent results reported from the first patient to be treated with the Leksell Gamma Knife (LGK) for MTLE encouraged the use of SR.[16]

The only article on the use and long-term results of SR in the treatment of MTLE published to date has given favorable epileptologic results.[17] Other reports failed to demonstrate the comparable effect of SR on microsurgical entorhinoamygdalohippocampectomy in patients treated with 25 Gy, 20, and 18 Gy to the 50% isodose line during either short- or long-term follow-up. These results are in accordance with some previously published studies, which are based on a lower number of treated patients and shorter follow-up periods The principal objections to studies on SR in MTLE published so far have included short delays between SR and indications for microsurgical operations and the short follow- up periods of irradiated patients.

SR do not lead to seizure control in group of patients; it led to transient seizure worsening in some of them and was associated with the risk of brain edema and intracranial hypertension. SR for MTLE does not exclude the possibility of a later epileptosurgical intervention.[18]

Deep brain stimulation

Electrical deep brain stimulation (DBS) via an implanted neurostimulator system is a promising therapy for epilepsy. The selection of the anterior nuclei (AN) as test sites was based on several factors, which include the initially positive results in the studies of Cooper, three unblinded pilot trials before Kerrigan et al, and subsequently, three after the randomized study, which showed approximately 50% seizure reduction.[19, 20, 21, 22, 23] Stimulation of the AN, which projects both to superior frontal and temporal lobe structures commonly involved in seizures, produces electroencephalography (EEG) changes and inhibits chemically induced seizures in laboratory models.

SANTE study demonstrated a beneficial and sustained effect on seizure frequency of bilateral AN DBS.[24]

Improvement rates observed compare favorably with a mean 47% improvement in 28 participants participating in six small uncontrolled studies of AN stimulation.[20, 21, 22, 23] By 2 years of stimulation, seizures were reduced by a median 56%, a 50%-responder rate improvement occurred in 54% of patients, seizures were less severe, and quality-of-life was improved.

Mechanisms of action of DBS are under study, but remain little understood. Why electrical stimulation of thalamus reduces seizures remote from the stimulation site is presently unknown. Subjects with temporal origin of seizures achieved relatively greater benefit of stimulation during the blinded phase, compared to those with seizures from other lobes or seizures multifocal in origin. Benefit to those with temporal seizure foci may reflect participation of mesial temporal lobe along with the AN of thalamus in the limbic circuit of Papez.

CONCLUSION

Surgical treatment of temporal lobe epilepsy still remains superior to all other treatment options. Further randomized prospective multicenter studies are warranted to obtain more results regarding other treatment modalities.

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