Epilepsy Surgery – candidates, preparations, results

MARKO ZORIĆ
UNIVERSITY OF ZAGREB SCHOOL OF MEDICINE

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SUMMARY: Epilepsy is a chronic disease that affects the nervous system and is characterized with seizures. It can be treated in the great majority of patients with antiepileptic drugs (AED). Unfortunately, there is a smaller group of patients, according to some researches about one third of patients, who have pharmacoresistant epilepsy and they cannot be treated even with a combination of two AED. These patients should be considered as potential candidates for neurosurgical treatment. A detailed neurological evaluation with functional and structural procedures like MRI (magnetic resonance imaging), EEG (electroencefalography), ictalSPECT (single photon emission computed tomography), positron emission tomography (PET), magnetoencephalography (MEG) is essential before conducting surgery. Some studies show promising results in neurosurgical treatment in the majority of cases but in the future bigger randomized studies from multicentric epilepsy centers should bring guidelines and standards for the choice of candidates for neurosurgery which will contribute to better outcomes.

KEYWORDS: Pharmacoresistant epilepsy, MRI, EEG, ictalSPECT, PET, MEG

Epilepsy is one of the most common neurological diseases. According to statistics from the Epilepsy foundation it is in the 4th position, only migraine, cerebrovascular stroke and Alzheimer disease are affecting more people1. It affects people worldwide with an estimated number of 50 million, and most of them are in developed countries. Epilepsy is a chronic disease that affects the nervous system and is characterized with seizures. Seizures are caused by the impairment of the electric activity of the brain or hyperstimulation. That triggers the excitation of some groups of neurons which we see as a seizure with tonic-clonic cramps but there can also be other symptoms such as lost of consciousness, sensations and auras[1]. According to the International League Against Epilepsy (ILAE) there are two big groups of epilepsy: partial seizures (simple or complex partial seizures,secondarily generalizing partial seizures) or generalized seizures (typical absence, atypical absence, mioclonic, tonic-clonic, tonic, clonic and status epilepticus)1. Seizures can also lead to death of millions of neurons because of the excitotoxic hyperstimulation, which must be taken seriously. Every seizure is a general risk for the health, chronic and repeatiosly seizures can cause serious brain damage and cognitive impairments.

Epilepsy can be treated in the great majority of patients with antiepileptic drugs (AED)[1]. There are several groups of them depending on their mechanism. The biggest problem is how to choose the proper dose, because the principal goal is to minimize the side effects and the seizures. Most patients can live without seizures while using AED, in general they use one but sometimes even two AED. Unfortunately, there is a smaller group of patients, according to some researches about one third of patients who develop pharmacoresistance and they cannot be treated even with two AED2. In that moment they should be considered as possible candidates for surgery. There are several reasons why they should have the option of surgery.

One of them is that every seizure is a very harmful condition that causes injuries, brain damages, vehicle accidents and sudden unexpected deaths in epilepsy (SUDIP) with an mortality rate of 1% per year[2]. The quality of life is, of course, very low because they cannot go to work, drive vehicles and many other activities, and that can lead to development of psychiatric disorders like depression, aggression or anxiety[2]. One of the most important factors is also the time or the duration of this condition. Because it is not the same if the surgery is made in the early stages of the disease when the results are much better and there are less functional and neurological impairments due to the seizures, or if the procedure is made after 10 or 20 years[2]. The surgical technique in the past 20 years has experienced many new breakthroughs and findings, so it is not considered as a very dangerous and high risk operation. A lot of epilepsy centers, which follow new trends in the treatment, have been established worldwide. Today is the risk of mortality for epilepsy surgery under 1% which is an average for neurosurgical procedures. Some complications as infections or unexpected bleeding do not differ from any other neurosurgical procedure and vary depending of the region[2].

In addition to that, the problem with farmacoresistant epilepsy is the definition which differs from one center to another, depending on the frequency of the seizures, their intensity, number of AED and the duration of unsuccessful medical treatment, use of AED after surgery, etc[3]. That can be the limitation in the results of surgery because we cannot compare two different groups or studies because of their very different parameters. That is why there is presently a definition which should be taken as the golden standard: Farmacoresistant epilepsy causes strong and frequent seizures that cannot be treated after a maximum dose of 2 AED in duration of at least 2 years[3].

Neurological evaluation

The presurgical evaluation and diagnostic protocol is also a problem, because there are no golden standards and there hadn't been any major multicentric studies that would give further

instructions in what to do if a patient has pharmacoresistant epilepsy. The question is how to choose the proper candidate among them, how good are the results of surgery, what are the potential risks and complications and what to do as a preoperative neurological and cognitive evaluation[2].

In the beginning it is very important to have an open and proper interview explaining the possible options and make realistic expectations for the surgical treatment[2]. It is also crucial to clearly explain the benefits and risks of the operation and give the opportunity to the patient to decide, or their parents and family if it is a child or a person with intellectual impairments[2]. The next step after the agreement is to assess the status of the patient and the disease which includes objective parameters (the number and intensity of the seizures, use of AED and their side effects) and subjective parameters (the patients view on their disability and the influence on their quality of life). After that the diagnostic and preoperative evaluation begins. The main goal of this step is to determine which type of epilepsy the patient has and in which region the "origin" of epilepsy is. In other words using various diagnostic tools we are trying to find the epileptogenic zone (EZ)[2].

Functional and structural diagnostic procedures

Firstly, an interview with the patient or the family or someone who witnessed the seizure can help a lot in localizing the epileptic foci depending on the preictal symptoms, auras etc[2]. A very useful tool in this case is electroencephalography (EEG), a neurophysiological procedure that detects and measures the electric activity of the brain using electrodes positioned on the scalp. This procedure can be also invasive if these electrodes are placed subdural or in the depth of the brain which is called stereoencephalography (SEEG). This invasive procedure is more commonly used in unclear situations when there is no obvious epileptogenic zone. For example, subdural electrodes can help in the detection of foci in cortical structures and SEEG in deep structures of the frontal and parietal lobe or the insular cortex[2]. Another interesting and helpful method is the video EEG monitoring which is a simultaneously long-term recording of the electric activity of the brain during sleep, awareness, the preictal and ictal period and it can lead to the localization of the EZ. The problem of this specific method are seizures that origin from the depth of the brain because, in that case, the video EEG monitoring can be misleading[2].

MRI (magnetic resonance imaging) is a diagnostic procedure to visualize the EZ and exclude some other causes of seizures: arterio-venous malformations, tumors or cortical dysplasia. A high quality MRI imaging requires a 3 Tesla MRI device and a neuroradiologist experienced in epilepsy who knows how to choose adequate sections and thickness[2]. The fMRI is necessary if the EZ is in an eloquent region e.g for speech, vision, sensorimotoric cortex and intraoperative brain mapping during the surgery should be considered as an option. It also helps to predict the dominant language hemisphere which could replace the Wada test in the future[2]. Wada test is a very invasive procedure of applying intracarotidal amytal to determine the dominant side for language and potential memory decline, which is very important for temporal lobe epilepsy especially for patients with mesial sclerosis[2].

A major role in future could be played by the ictalSPECT (single photon emission computed tomography). In these images ictal discharge zones are hyperperfused and surrounded with hypoprefused zones[2]. These findings, in correspondence with interictal images and together with MRI findings data called SISCOM (subtraction ictal SPECT coregistered with MRI), could help to precisely determine the EZ. Positron emission tomography (PET) using flurodeoxyglucose (FDG) shows the cell metabolism with the utilization of radioactive glucose[2]. Studies showed that in interictal periods lobes of hypometabolism are mostly lobes of ictal discharge and their importance lays in cases when MRI images do not show morphological abnormalities as a cause of epilepsy. A multichannel magnetoencephalography (MEG) is vastly improved in the last decade, and provides new data about the localization of cortical spikes in Landau-Kleffner syndrome and epileptogenic tubers[2]. Aside from that, this procedure does not involve the use of radioactive agents and it is less stressful than MRI which especially helps with children.

Surgical procedures, outcomes and results

The surgical types can be roughly divided into resective and functional surgery4. If we have the localization of the EZ the goal is to remove that zone via lobectomy or multiple subpial transaction which will lead to the disappearance of seizures. The other type is functional surgery which is used when we try to disconnect some structures like the corus callosum – callosotomy, thus disabling the spreading of the seizure into generalized types[4]. The second option for functional surgery is deep brain stimulation (DBS) which can be used in patients with no main or unclear EZ, mostly by implanting the electrode in the hippocampus, anterior thalamic nucleus or by vagal nerve stimulation[4]. These respective procedures in the temporal lobe have a high success rate and 70-80% of patients are seizure free whereas patients which underwent extratemporal procedures are 60-70%

seizure free4. Unfortunately, partial success is observed with procedures such as callosotomy, DBS or MST, in which case only 50% of patients show a lower frequency of seizures[4].
A Swedish national prospective study showed promising results[5]. They did a 5 and 10 year follow up of 278 patients after epilepsy surgery, and patients which didn't undergo surgery were the control group. The results showed that 62% of adults and 50% of children which underwent surgery were seizure free in comparison to the control group where 14% of nonoperated adults and 38% of nonoperated children were seizure free[5].
Among these, there is a possibility to treat epilepsy with radioneurosurgery- gamma knife[3]. Some neurosurgeons tried to treat mesial scloresois with this option when patients didn't want to undergo surgery or had contraindications[3]. The first results were promising without neurological deficits but brain swelling due to radiation had to be treated with dexamethason. Longer and bigger studies haven't been conducted but this option could be taken into consideration in the future[3].

Something that should also be taken care of are preoperative seizures due to lowered AED serum concentration, besides that it is more preferable to take the AED's enteral or intravenous before the scheduled neurosurgical operation, and some researches showed that anesthetics in low doses are proconvulsive but in higher doses they have anticonvulsive effects[2]. Other drugs can also affect the threshold for seizures for example opioids are strictly proconvulsive[6]. If the patient is undergoing other non-neurosurgical procedures, diagnostic or therapeutic, with local or general anesthesia (tonsillectomy, biopsies, etc.) these things should be discussed between the anesthesiologist and neurologist6. Good assessment and evaluation by the neurologist can avoid almost all potential preoperative seizures and complications without any risk of seizures after the surgical or diagnostic procedure; they require also no special AED's and benzodiazepines are enough for profilaxy[6].

Conclusion

To summarize, epilepsy surgery has made big improvements and the number of the types of epilepsy which can be successfully treated is rapidly growing. The goal of the neurological evaluation is to use all these methods in order to give answers to several questions: is this seizure epileptic, where is the cause of it or EZ and is it treatable with AED or surgery. If the answer is surgery the next step is to choose which type of surgery could be curative and what are the potential outcomes. In the future new multicentric studies from specialised epilepsy centers

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Operacija epilepsije- kandidati, priprema, rezultati

SAŽETAK: Epilepsija je kronična bolest koja zahvaća središnji živčani sustav i karakterizirana je epileptičkim napadajima. U većini slučajeva se može uspješno liječiti lijekovima - antiepilepticima. No nažalost postoji dio pacijenata, oko jedne trećine koje imaju farmakorezistentni oblik koji se ne može liječiti niti s kombinacijom dva antiepileptika. Njima bi trebalo ponuditi mogućnost neurokirurškog liječenja. Detaljan neurološki pregled koji uključuje niz pretraga kao što su MRI, EEG, iktalniSPECT, PET i MEG su ključni prije samog zahvata. Studije pokazuju uspjeh kod većine neurokirurški liječenih pacijenata ali u budućnosti bi trebale velike multicentrične studije dati jasne smjernice za pristup i izbor kandidata za operativno liječenje.

KLJUČNE RIJEČI: Farmakorezistentna epilepsija, MRI, EEG, ictalSPECT, PET, MEG