Why Consider Early Epilepsy Surgery?
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Background

Various epilepsy surgery procedures can be used to cure or reduce seizure frequency. Most procedures are either designed to resect or disconnect the area of the brain where seizures originate or spread. Epilepsy surgery is a procedure that either removes or isolates the area of the brain where seizures originate. Epilepsy surgery can significantly improve seizure control in a carefully selected group of individuals. Seizure freedom can be as high as 70-80%, and a large percentage of patients can have a significant reduction in seizure frequency or disabling seizures following surgery. However, referral for evaluation often is delayed and occurs years later after numerous medications have been tried. Unfortunately, it often takes 20 years for a patient to be referred for evaluation for epilepsy surgery.

Worldwide, referral for epilepsy surgery is underutilized. Less than 1% of patients with treatment resistant epilepsy are referred for a surgical evaluation. Lack of knowledge by physicians of the benefits of surgery and appropriate surgical candidates, fear of complications, and the thought that people may outgrow the epilepsy at a later time are some of the reasons. Another reason could be due to physicians’ perception of epilepsy surgery as a “last resort” procedure.

In British Columbia, 40,000 individuals have epilepsy. Approximately 30% have treatment resistant epilepsy. Therefore, 3000-5000 patients in our province could benefit from epilepsy surgery.

Natural history of epilepsy and response to medication

One of the main arguments for early epilepsy surgery is the observation that once seizures do not respond to treatment (treatment resistant), the chance of seizure freedom with further medication trials is small. One study looked at patients who had epilepsy for at least 5 years and at least one seizure per month. Of those who had tried less than five medications, 24% seizures were controlled with expert treatment. In comparison, only 11% of those who had tried five or more medications became controlled (1). This is obviously dependent on the cause of seizures and the epilepsy syndrome. Children may have a higher response rate to medications. Also, the introduction of newer anti-seizure medications may slightly change these numbers. Resistance to medications may remit over time (at a rate of 4% per year among adults and a higher rate among children). However, seizure relapse is common, suggesting epilepsy can have a fluctuating course (2).

Kwan and Brodie reported that those who have many seizures before therapy or who have an inadequate response to initial treatment with anti-seizure medications are likely to have treatment resistant epilepsy. They found that 47% became seizure free with their first anti-seizure medication and 14% became seizure free during treatment with a second or third medication. Among patients who had no response to the first medication, the percentage that subsequently became seizure free was smaller (11%) when treatment failure was due to lack of efficacy than when it was due to intolerable side effects (41%) (3).

Consequences of uncontrolled seizures

The goals of epilepsy surgery are to decrease seizure frequency or to render patients seizure free sooner with better success than medical therapy. Surgery in children also aims to prevent the negative effects of seizures on brain development and to improve quality of life in the child and family. Better and earlier seizure control should reduce seizure associated morbidities.

Mortality

Uncontrolled frequent seizures are associated with an increased risk of death. Sudden unexplained death in epilepsy (SUDEP) rates are quoted to be the highest in surgical series patients with treatment resistant epilepsy
compared with community prevalence samples (4). Lower mortality has been consistently observed among
patients who are seizure free by surgery compared with both surgical patients who have persisting seizures and
patients who were evaluated for but did have surgery.

**Cognitive decline**

Seizures can have a negative effect on brain development and learning especially in children. Good seizure
control, even after years of treatment resistance, can have a beneficial impact on cognition (5).

With temporal lobe epilepsy, in cross-sectional studies memory is worse in patients with a longer duration and
earlier age at onset of epilepsy (6). In one longitudinal study, surgery abolished or reversed the decline in memory
function (7). In another study, 25-40% of treatment resistant patients showed decline on tests of confrontation and
naming compared to friend or relative controls (8).

It also known that frequent seizures can lead to “pseudo-regression” where the seizures and medications impact
sleep, energy, attention, mood, learning and interaction with the environment. This is thought to be reversible with
better seizure control.

**Effectiveness of epilepsy surgery**

Evidence for the effectiveness of epilepsy surgery has been shown in one randomized controlled trial in temporal
lobe epilepsy. 58% of surgically treated patients were seizure free at one year compared with 8% of medically
treated patients (9). The resulting practice guideline by the American Academy of Neurology, the American
Epilepsy Society and the American Association of Neurological Surgeons recommends that those with partial
seizures who failed first-line anti-seizure medications should be referred to an epilepsy surgery center, and that
those who meet the criteria for mesial temporal resection should be offered surgery. There is evidence for
success of epilepsy surgery from other areas of the brain also.

The success rates of surgery are dependent on several factors, such as the presence or absence of a lesion,
seizure etiology, area of seizure onset, concordance of other tests, etc.

Self-reported quality of life (QOL) studies consistently show improvements with postsurgical seizure control. The
results are not so favorable when seizures persist (10, 11).

**Risks of epilepsy surgery**

As is true for any surgery, brain surgery has risks. General risks of surgery include complication of anesthesia,
bleeding and infection. A more serious infection, meningitis, can occur after brain surgery. This is an infection of
the layers that cover the brain. Brain swelling can also occur and lead to headache and discomfort. The surgeon
will often prescribe a medication to reduce the risk of swelling after surgery. Rarely, a vascular injury can occur
intraoperatively and this can lead to a stroke. The risks are dependent on the area and extent of the resection.
Investigations, such as cortical stimulation or mapping brain function, neuropsychological evaluation and
functional MRI, can predict and determine the risks of neurological deficit prior to surgery. In one meta-analysis of
temporal lobe resections, dysphasia or speech alteration occurred in 3%, weakness on one side of the body
occurred in 2%, and large visual field defects occurred in 2%. Of these, half were permanent. Death was reported
in 0.4% and was unrelated to surgery (12).

Declines in verbal memory and word finding are the most common cognitive side effects, occurring in up to 40%
of patients with temporal lobe resections. However, these are often known with the pre-surgical work-up, and the
risks versus benefits are discussed with the patient (13). Of note, memory decline has been associated with a
decline in the quality of life when seizures persist (14).

**Cognitive outcomes of epilepsy surgery**

Early surgery may reduce cognitive morbidity by preventing progression associated with frequent seizures. Timing
may be very important, as younger brains may have a greater capacity for plasticity or “rewiring” of function and
therefore better recovery. Some believe that the long-term cognitive trajectory after surgery may be related more
to progression of the underlying disease than to seizure control. Early surgery could be most beneficial if it could
decrease or halt progression of the underlying disease.
There are not many studies comparing epilepsy surgery in adults and children. One study compared cognitive tests between groups of children and adults. Adults and children with a left sided resection showed expected mean declines in verbal memory at three months following surgery. By one year, the mean scores for children were no longer different from pre-surgical scores, but adult scores remained below their pre-surgical mean (15). This exemplifies the potential benefits of early surgery.

**Conclusion**

The evidence for performing surgery earlier is persuasive. It is known that late remissions with medical treatment are less likely. The data regarding the impact of uncontrolled seizures on morbidity, quality of life, mortality, and social and cognitive functions supports early surgery.

Also, the efficacy and safety of surgery have been established in patients. However, the optimum timing of surgery has not been fully determined. Treatment resistance and consideration for surgery does not develop at a uniform time in surgical candidates, and late remissions are still possible. Ultimately, the goal is to reduce seizure frequency, optimize quality of life, and reduce morbidity and mortality as soon as possible. Good prospective studies looking at standardized interventions and outcomes are necessary. However, evidence to date suggests benefits of early epilepsy surgery in appropriate candidates.

**References**