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Predicting outcome following reoperation for medically intractable epilepsy

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The purpose of this study was to determine predictors of probable outcome following reoperation for medically intractable partial epilepsy. We reviewed outcome at least 1 year after reoperation in 21 patients with intractable seizures, for whom an earlier operation had failed. We examined age of onset of epilepsy, duration of seizures, gender, details of the history and clinical examination, pre-operative magnetic resonance (MRI) findings, electroencephalographic (EEG) studies obtained before and after the failed surgery, presence or absence of lateralizing neuro-psychological deficits, sites of operation and pathology of resected tissue to identify the factors associated with outcome. We found two factors that were significantly related to outcome: (1) no individual with a history of central nervous system (CNS) infection which predated the onset of epilepsy had a seizure-free outcome after reoperation ($P = 0.04$). (2) Reoperations that extended previous resections, based on new ictal EEG recordings that were concordant with both EEG ictal onsets and MRI findings obtained before the first, failed surgery resulted in a seizure-free outcome or >95% reduction in seizures for 100% (7/7) of such patients. This compares to 29% (4/14) of the remaining individuals without such concordance who had a similar outcome ($P = 0.009$). Site of operation (temporal or extratemporal) did not, in and of itself, predict outcome. A portion of patients who fail surgery for intractable partial seizures will achieve significant improvement following reoperation. Furthermore, we may be able to identify those individuals most likely to have an excellent result from a second operation.

Key words: intractable epilepsy; epilepsy surgery; reoperation.

INTRODUCTION

The surgical treatment of medically intractable partial epilepsy is of highly significant benefit in carefully selected cases, with a seizure-free outcome expected for the majority of patients for whom such treatment is recommended[1]. When epilepsy surgery fails, however, it is difficult to decide whether or not to consider reoperation. Given the risks attendant to neurosurgical procedures, as well as the not inconsiderable costs required for evaluating and treating surgical candidates, it is reasonable to question the utility of reoperation[2]. Ideally, one would like to consider for repeat epilepsy surgery those patients for whom the likelihood of success is substantial, and eliminate from consideration those patients for whom there is little likelihood of success. By examining our series of patients who have undergone more than one operation for epilepsy, we find that we may be able to predict, in some cases, the probable outcome of another operation.

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MATERIALS AND METHODS

We studied 21 patients who were evaluated and treated at our institution for medically intractable partial epilepsy and who underwent more than one operation for control of seizures. All patients underwent reoperation between 1991 and 1996, representing less than 5% of all patients who underwent epilepsy surgery at the University of Washington during that time.

All patients experienced medically intractable complex partial seizures, with or without secondary generalization. Average age at the time of the first surgery was 22 years (range 6–41), with an average duration of

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seizures prior to the first operation of 15 years (range 2–36). The age of onset of seizures ranged from birth to 33 years; 52% (11/21) of the patients were male.

Risk factors for seizures included a history of CNS infection (meningitis or encephalitis) in four patients, head injury with loss of consciousness in six, and febrile seizures[3] in three. Six patients exhibited focal neurological signs. Standard pre-operative interictal EEGs disclosed unilateral focal spikes for 43% (9/21) of the patients; the remainder showed bilateral or multifocal discharges. Pre-operative brain MRI studies disclosed unilateral hippocampal atrophy in four patients, calcified temporal lobe masses in two patients, extratemporal encephalomalacia in three, posterior atrophy in one, hemispheric dysplasia in one, frontal porencephaly in one, porencephaly and ipsilateral hemispheric atrophy in one, diffuse atrophy in one, and ventricular calcification in one. The MRIs of six patients were normal. Neuropsychological deficits lateralized more to the left hemisphere in nine patients, to the right in four, and were nonlateralizing in six. Cerebral angiogram with intracarotid sodium amobarbital testing was performed in most patients to determine the side of speech production and competency of memory function contralateral to the proposed side of surgery[4].

Ictal EEG recordings were obtained for all patients, including eight patients who underwent intracranial subdural cortical strip or grid monitoring pre-operatively. The surgical technique was that of a tailored resection in all cases[5]. Strictly temporal resections were performed in 52% (11/21) of the patients, with the remaining 48% (10/21) also including extratemporal resections. Gliosis was the pathologic diagnosis in 86% (18/21) of the patients, while ganglioglioma, neuronal dysplasia, and increased vascularity with gliosis were diagnoses established for one patient respectively.

No patient experienced complete control of seizures following the first operation and all were considered candidates for reoperation. Prior to another operation, we obtained new surface ictal EEG recordings; intracranial strip or grid studies were also obtained for 52% (11/21) of the patients. Ictal onsets for 19% (4/21) arose from the same cerebral hemisphere, but different lobes, when compared with the sites of the initial operations, while seizures arose from the same region in 81% (17/21) of the patients. We planned subsequent operations based on the new ictal recordings, and extended previous resections in 81% (17/21) of the patients. Reoperations included multiple subpial transections[6] in two patients, where ictal onsets involved motor cortex, completion of hemispherectomies[7] in two children, and focal resections for the remainder. For the temporal reoperations, hippocampal resections were extended in four, lateral resections extended in four, and both hippocampal and lateral resections extended in three patients. There were no operative complications. The interval between operations averaged 2 years (range 0.5–4). One male patient underwent three operations: after two cortical topectomies had failed he underwent resection of the ipsilateral insula, based on ictal single photon emission computed tomographic studies[8], and became seizure-free after the third operation. We did not consider for reoperation those few patients where ictal onsets after surgery came from the side opposite to the operation.

We compared reduction in seizures in the year following the final operations to the seizure frequency in the year before the final surgery. We included all seizures, including simple partial seizures, regardless of circumstances such as antiepileptic drug withdrawal. We examined age of onset of seizures, duration of epilepsy, gender, details of history and physical findings, pre-operative MRI findings, EEG studies obtained before and after the failed operation, presence or absence of lateralizing neuropsychological deficits, site of operations, and pathology of resected tissue to determine any relationship between these variables and outcome following repeat surgery.

RESULTS

We followed patients for an average of nearly 3 years following reoperation (range 1–5). All had at least 1 year of follow-up. There were no short-term follow-up cases who underwent repeat surgery during the interval covered in this study. Overall, 43% (9/21) patients of the patients were completely seizure-free. Two patients (9%) had more than 95% reduction in seizures (and less than one seizure monthly), while 24% (5/21) had more than a 75% reduction in seizures during the follow-up period. The remaining 24% (5/21) of the patients were found to have less than 75% reduction in seizures.

We found that age of onset of seizures, gender, duration of epilepsy, clinical examination findings, standard pre-operative EEG findings, site of surgery (temporal vs. extratemporal), lateralizing neuropsychological deficits, and pathology of resected tissue had no relationship to outcome.

We found that two factors did have a significant influence on outcome: (1) none of the four patients with a history of CNS infection that preceded the onset of epilepsy was seizure-free or had more than a 95% reduction in seizures following reoperation ($P = 0.04$, Fisher's Exact test, two-tailed). Other risk factors for epilepsy, including head trauma and febrile seizures in childhood, had no significant relationship to outcome. (2) Concordance of focal abnormal findings on pre-operative MRI with ictal EEG onsets obtained before and after the first failed surgery led to a seizure-free

Table 1: Relationship between outcome after reoperation and degree of concordance with initial MRI findings and ictal EEG onsets before and after the first failed surgery*.

Outcome	Group 1 ($n = 7$)	Group 2 ($n = 14$)
Seizure-free	5 (72%)	4 (28%)
>95% reduction in seizures	2 (28%)	0
>75% reduction in seizures	0	5 (36%)
<75% reduction in seizures	0	5 (36%)

* $P = 0.009$, Fisher's Exact test.

Group 1, Reoperations extending previous resections based on ictal EEG onsets concordant with ictal EEG onsets and MRI findings before the first failed surgery

Group 2, Reoperations based on ictal EEG onsets discordant with previous ictal EEG or MRI, or in cases of normal pre-operative MRI.

outcome or more than a 95% reduction in seizures in 100% (7/7) of patients where such concordance was found. These results are in contrast to those patients who had normal pre-operative MRI studies, discordant MRI findings and EEG ictal onsets, or ictal onsets before reoperation that differed from ictal onsets obtained before the first surgery. For this group, only 29% (4/14) were either seizure-free, or had more than a 95% reduction in seizures after reoperation ($P = 0.009$, Fisher's Exact test). Table 1 summarizes the relationship between outcome after reoperation and the degree of concordance between initial MRI findings and ictal EEG onsets before and after the first failed surgery.

DISCUSSION

The indications for reoperation in the treatment of medically intractable epilepsy are dictated by the original indications for surgery[9]. If surgery fails initially, some patients may still be eligible for operative therapy. Previous reports have indicated that 33–63% of patients can expect complete or nearly complete cessation of seizures following reoperation[9–14]. What is less clear is which patients are most likely to benefit from another operation.

Some authors emphasize that reoperations are most likely to result in a good outcome if such procedures involve extending previous resections. In particular, resecting residual mesial-basal structures in patients with temporal lobe epilepsy has frequently resulted in a good outcome[10–12]. While some reports indicate that reoperation for temporal lobe epilepsy is more likely to result in a good outcome than extratemporal epilepsy, patients with incompletely resected extratemporal structural lesions have also been shown to have complete or significant amelioration of seizures after reoperation[10]. Investigators have also noted ictal onsets which prove to originate from cortical sites different from that observed before the first operation usually portend a less satisfactory outcome following repeat surgery than ictal onsets arise from the resected region[11].

A pattern that emerges from these earlier studies on reoperation for drug-resistant epilepsy is the observation that better outcomes may be found in those individuals who had concordant electrographic ictal onsets before and after the first failed surgery. Our results to a large degree, affirm this pattern. However, we find that even more precise predictions of outcome can be achieved by carefully considering other variables as well.

To our knowledge, specific risk factors for epilepsy have not been implicated as having any effect on outcome following reoperation. We find that a history of CNS infection adversely influences outcome following following repeat surgery. One may speculate that such infections, by frequently producing bilateral brain injury, are less likely to leave focal, unilateral, and concordant electrographic and imaging abnormalities. Hence, should seizures be sequelae of infection, patients so afflicted may not be favourable candidates for reoperation. Whether or not a history of CNS infection adversely affects outcome for epilepsy surgery in general is controversial. While some investigators believe a history of CNS infection has no deleterious relationship to outcome after epilepsy surgery[15], others find that such a history, by frequent association with neocortical epilepsy and normal MRI, is often found in patients with relatively poorer surgical results[16].

In general, concordance of focal lesions on MRI with electrographic ictal onsets is clearly an important predictor of good outcome in patients with intractable temporal lobe epilepsy referred for surgical therapy[17, 18]. In addition, in patients with intractable frontal epilepsy outcomes after surgery are better for those with MRI lesions compared to those without[19].

We find that the principle of concordant imaging and EEG data as a good predictor of outcome in epilepsy surgery in general can be extended to individuals considered for reoperation. We find that it does not matter, *per se*, whether seizures are temporal or extratemporal in origin. Rather, it is more important to determine if seizures arise from the region of previous resection, and if ictal onsets converge with the pre-operative MRI. As a result of such careful determinations, coupled with knowledge of the risk factors, we may reasonably be able identify patients with intractable epilepsy who will most likely have an excellent outcome after another operation and those who will probably not.

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