Seizure Types and Frequency in Patients Who "Fail" Temporal Lobectomy for Intractable Epilepsy

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> n 30% of patients with temporal lobe epilepsy (TLE), the most common epilepsy syndrome, seizures are refractory to antiepileptic drugs, leading to significant morbidity and even mortality. ^{I-3} Class I evidence has demonstrated that temporal lobectomy is an effective treatment for

ABBREVIATIONS: AED, antiepileptic drug; CPS, complex partial seizure; ECoG, electrocorticography; EEG, electroencephalography; GTCS, generalized tonic-clonic seizure; SPS, simple partial seizure; TLE, temporal lobe epilepsy; UCSF, University of California, San Francisco

intractable TLE, and 60% to 80% of patients achieve freedom from disabling seizures after surgery. 4,5 Most clinical studies of temporal lobectomy evaluate rates and predictors of postoperative seizure freedom, and patients who continue to have seizures after resection are routinely considered to have "failed" surgical therapy. 6,7 There is some merit to an all-or-none viewpoint of epilepsy surgery outcomes, because, indeed, seizure freedom is the single most important predictor of quality of life after epilepsy surgery.^{8,9} Owing in part to this perspective, however, less is known about the specific seizure types and frequencies that continue to occur in patients who "fail"

BACKGROUND: Temporal lobectomy can lead to favorable seizure outcomes in

medically-refractory temporal lobe epilepsy (TLE). Although most studies focus on

seizure freedom after temporal lobectomy, less is known about seizure semiology in

patients who "fail" surgery. Morbidity differs between seizure types that impair or spare

consciousness. Among TLE patients with seizures after surgery, how does temporal lobectomy influence seizure type and frequency? **OBJECTIVE:** To characterize seizure types and frequencies before and after temporal lobectomy for TLE, including consciousness-sparing or consciousness-impairing seizures. METHODS: We performed a retrospective longitudinal cohort study examining patients undergoing temporal lobectomy for epilepsy at our institution from January 1995

RESULTS: Among 241 TLE patients who received temporal lobectomy, 174 (72.2%) patients achieved Engel class I outcome (free of disabling seizures), including 141 (58.5%) with complete seizure freedom. Overall seizure frequency in patients with persistent postoperative seizures decreased by 70% (P < .01), with larger reductions in consciousness-impairing seizures. While the number of patients experiencing consciousness-sparing simple partial seizures decreased by only 19% after surgery, the number of individuals having consciousness-impairing complex partial seizures and generalized tonic-clonic seizures diminished by 70% and 68%, respectively (P < .001). Simple partial seizure was the predominant seizure type in 19.1% vs 37.0% of patients preoperatively and postoperatively, respectively (P < .001). Favorable seizure outcome was predicted by a lack of generalized seizures preoperatively (odds ratio 1.74, 95% confidence interval 1.06-2.86, P < .5).

CONCLUSION: Given important clinical and mechanistic differences between seizures with or without impairment of consciousness, seizure type and frequency remain important considerations in epilepsy surgery.

KEY WORDS: Consciousness, Epilepsy surgery, Outcomes, Seizure types

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temporal lobectomy. Because different seizure types have variable impact on patients, a better understanding of seizure burden after "failed" temporal lobectomy will offer insight into the full impact of surgery.

In TLE, seizures may include both partial and secondarily generalized events. 10 Generalized tonic-clonic seizures (GTCSs) are the most severe self-limited seizure type, in which seizure activity propagates from the temporal lobe to widespread bilateral cortical regions, causing loss of consciousness, convulsive motor activity, and postictal confusion. 11 Frequent GTCSs also increase the risk of sudden unexplained death in epilepsy. 12,13 Among partial seizures in TLE, complex partial seizures (CPSs) are the most common form. Similar to GTCSs, they are associated with impaired consciousness and sometimes involve motor activity such as facial automatisms. 14 Simple partial seizures (SPSs) are the least severe seizure type, during which consciousness in spared. 14 SPSs include simple motor seizures and include isolated auras, which typically occur in a few characteristic patterns in TLE, as we have previously described. 15 Consciousness-impairing seizures in TLE can lead to significant morbidity, including motor vehicle accidents, drownings, diminished work and school performance, and decreased quality of life. 16-20 Furthermore, neuroimaging and electrographic studies have revealed substantial differences in brain network activity during partial seizures involving spared vs impaired consciousness. Intracranial electroencephalography (EEG) and single positron emission computed tomography studies of TLE have shown that CPSs are associated with depressed frontoparietal neocortical function and aberrant subcortical and brainstem activity, whereas abnormal network activity in SPSs appears confined to the temporal lobe of origin. ^{21,22} Temporal lobectomy disrupts these seizure networks, completely halting seizures in the most fortunate patients. However, among individuals who continue to have postoperative seizures, the effects of temporal lobectomy on consciousness-sparing vs consciousnessimpairing seizures have not been directly examined.

Here, we present a retrospective cohort study examining temporal lobectomies for TLE performed at our institution over an approximately 15-year period. We investigate not only predictors of Engel class I seizure outcome, but also seizure types and frequencies in patients who do not achieve seizure freedom.

PATIENTS AND METHODS

Data Collection

We reviewed the medical records of 265 consecutive temporal lobectomy procedures performed in 260 patients with medically refractory TLE at the University of California, San Francisco (UCSF) between January 1995 and August 2010. The study design was a retrospective longitudinal cohort investigation of seizure outcomes among patients receiving temporal lobectomy for intractable epilepsy. Postoperative follow-up of at least 1 year was required, and study duration for each patient ended with last follow-up (ie, there was no fixed study duration). Nineteen patients without at least 1 year of postoperative follow-up at our institution were excluded, and data for the remaining 241 patients were analyzed. All aspects of the study were in compliance with the UCSF Clinical and Translational Science

Institute policies, and research protocols were approved by the UCSF Committee on Human Research.

The decision to proceed to surgery was made by a comprehensive team at the UCSF Epilepsy Center, including adult and pediatric epileptologists, neurosurgeons, neuroradiologists, neuropsychologists, and other practitioners. Standard preoperative workup included structural magnetic resonance imaging (MRI), EEG, neuropsychology evaluation; and the workup often also included magnetoencephalography, positron emission tomography, WADA testing of language and memory lateralization, and long-term video/EEG monitoring with or without surgically implanted subdural and depth electrodes, in addition to standard surgical and anesthesiologic evaluation. Anterior temporal lobectomy was performed by 1 of 4 neurosurgeons, with resection including the anterior middle and inferior temporal gyri, anterior hippocampus, and amygdala. Resections were customized to incorporate regions of identified epileptogenic zones and/or cerebral lesions, and to preserve eloquent cortex, where applicable. Intraoperative electrocorticography (ECoG) was used in approximately half of surgeries to further guide resection. Awake intraoperative language mapping using direct cortical stimulation was used for appropriate candidates when the resection involved the dominant hemisphere. Surgical specimens were analyzed by neuropathologists.

Inpatient and outpatient provider notes, diagnostic and laboratory reports, and operative records were reviewed. We recorded patient age, sex, handedness, duration of epilepsy, antiepileptic drug (AED) use history, surgical history, neuroimaging results, EEG results, use of implanted intracranial electrodes for long-term recording, details of resection extent, side of surgery, use of intraoperative ECoG, and pathological findings. Details regarding the patient's epilepsy history and seizure semiology, including seizure type and frequency, were obtained from preoperative and postoperative charting performed by epileptologists. Specific seizure types tracked included GTCSs (bilateral convulsive activity with loss of consciousness and postictal impairment), CPSs (partial seizures without convulsion but with impairment of consciousness, awareness, or ability to interact during the event), and SPSs (partial seizures with preserved consciousness). Isolated auras, which are considered a type of SPS, 23,24 were included as such. Epilepsy risk factors were recorded and tallied, including history of (1) birth injury or cerebral palsy, (2) static encephalopathy or developmental delay, (3) head trauma, (4) febrile seizures, (5) central nervous system infection, (6) family history of epilepsy, (7) alcohol or drug abuse, (8) cerebral ischemia, and/or (9) status epilepticus. Seizure outcome as of latest follow-up with the epileptologist was determined by using a modified Engel classification system. ²⁵ In brief, patients with no residual seizures were classified as Engel IA, those with rare residual nondisabling consciousness-sparing seizures were considered Engel IB-D, patients with rare disabling consciousness-impairing seizures were labeled Engel II, and individuals with or without worthwhile improvement were considered Engel III or IV, respectively.

Statistical Analysis

Individual seizure types and the predominant seizure type (defined as the seizure type experienced most commonly for each patient) among patients before vs after surgery were compared by using χ^2 tests. T tests were used to compare preoperative and postoperative seizure frequencies among individuals with persistent seizures. To analyze factors associated with more favorable seizure outcome (ie, seizure-free or only rare consciousness-sparing seizures, Engel IA-D) vs less favorable outcome (ie, persistent consciousness-impairing seizures, or Engel II-IV), we used χ^2 tests for categorical variables (eg, sex) and an unpaired Student t test

for continuous variables (eg, age). Before using parametric tests, normality of data was verified, and the Levene test for equality of variances was applied. For multivariate analysis of factors associated with more favorable seizure outcome, variables were dichotomized (continuous variables dichotomized at approximately the median) and entered into a Cox regression analysis with follow-up duration as the time-related variable. Odds ratios were calculated with a 95% confidence interval. Statistical significance was assessed at P < .05. All statistical analyses were performed by using SPSS version 20 (IBM, Somers, NY).

RESULTS

Patient Demographics and Seizure Outcomes

Among 265 temporal lobectomies in 260 TLE patients during the study period, 241 individuals had mean postoperative follow-up (\pm standard error of the mean) of 3.5 \pm 0.2 years (range, 1-13), and the remaining 19 (7.3%) were excluded. Patients were 52.7% female, with a mean age of 34.7 \pm 0.9 years (range, 4-74) and mean duration of epilepsy of 20.1 \pm 0.8 years at the time of surgery. Individuals had failed a mean of 4.2 \pm 0.1 different AEDs (range, 2-12) before surgery. Thirteen patients (5.4%) had a previous temporal lobe resection, and 3 (1.2%) had received vagus nerve stimulator implantation. Other patient and surgery characteristics are summarized in Table 1.

As of the latest postoperative follow-up, 174 (72.2%) patients achieved an Engel class I outcome, including 141 (58.5%) individuals who became completely seizure-free (Engel IA), and 33 (13.7%) patients who were free of all disabling seizures (Engel IB-D). Otherwise, 40 (16.6%) patients achieved Engel class II seizure outcome, 16 (6.6%) individuals had class III outcome, and 11 (4.6%) patients had class IV outcome. Final pathology

TABLE 1. Patient and Surgery Characteristics ^{a,b}	
Age at surgery, y, mean \pm SEM	34.7 ± 0.9
Male	47.3
Right handed	88.8
Right-sided surgery	49.4
Previous resection	5.4
Epilepsy duration, y, mean \pm SEM	20.1 ± 0.8
History of generalized seizures	30.7
Abnormal MRI	91.6
Localizing ictal EEG	82.4
Implanted electrodes used	35.1
Intraoperative ECoG used	45.9
Pathology	
MTS	46.9
Normal/gliosis only	18.7
Tumor	14.5
Cortical dysplasia	6.6
Other	13.3

^aEEG, electroencephalography; ECoG, electrocorticography; MRI, magnetic resonance imaging; MTS, mesial temporal sclerosis; SEM, standard error of the mean.

confirmed mesial temporal sclerosis in 46.9% of patients, showed normal tissue or only gliosis in 18.7% of cases, and found tumor in 14.5% of cases (Table 1). Fifteen (11%) completely seizure-free patients had discontinued all AED use for ≥ 1 year by latest follow-up. There was no perioperative mortality.

Effects of Surgery on Consciousness-Sparing and Consciousness-Impairing Seizures

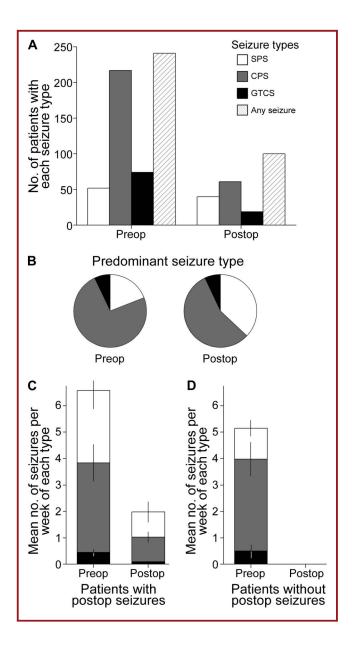
Next, we examined seizure types in patients before and after surgery, including seizures associated with altered consciousness (CPSs and GTCSs) or preserved consciousness (SPSs, including isolated auras). Although the number of patients experiencing SPSs decreased by only 19% after surgery, the number of individuals having CPSs and GTCSs diminished by 70% and 68%, respectively $(\chi^2 = 16.9, P < .001)$ (Figure A). Furthermore, although SPS was the predominant seizure type in only 19.1% of all patients before surgery, it was more frequently (37.0%) the predominant seizure type among patients with postoperative seizures ($\chi^2 = 11.4$, P < .01) (Figure B). This trend was observed whether or not patients who achieved postoperative seizure freedom were removed from the analysis of preoperative data. This suggests that in patients who are not seizure free postoperatively, temporal lobectomy may have greater impact on consciousness-impairing seizures than on consciousness-sparing seizures.

We also assessed pre- and postoperative frequencies of all seizure types (Figure C and D). Compared with preoperative baseline, patients with continued seizures after lobectomy experienced SPSs 65% less frequently (unpaired Student $t=2.9,\ P<.01$), CPSs 73% less often ($t=2.4,\ P=.02$), and GTCSs 78% less often ($t=1.3,\ P=.19$), leading to a 70% decrease in overall seizure frequency ($t=3.0,\ P<.01$) (Figure C). Notably, preoperative baseline seizure rates did not differ significantly between patients who ultimately did achieve seizure freedom (Figure D) vs those who did not (Figure C) (P>.15 for all comparisons). These results suggest that temporal lobectomy leads to a significant decrease in seizure frequency among patients who continue to seize postoperatively.

Predictors of Seizure Outcome

Next, various patient characteristics were examined for potential association with more favorable seizure outcome (ie, seizure-free or only rare consciousness-sparing seizures, Engel IA-D) vs less favorable outcome (ie, persistent consciousness-impairing seizures, or Engel II-IV) (Table 2). Univariate analysis revealed that favorable seizure outcome was significantly more common in patients without generalized seizures, and in those with an abnormal preoperative MRI, compared with individuals with a history of generalized seizures or a normal MRI, respectively (Table 2). No difference in mean follow-up time was observed between patients with more favorable vs less favorable outcome (t = -1.2, P = .25). Finally, Cox regression was performed for longitudinal multivariate analysis of potential predictors of favorable seizure outcome. Favorable seizure outcome was significantly predicted by a lack of preoperative generalized

^bAll values represent percentage of patients, except where otherwise indicated.



seizures compared with a positive history of generalized seizures (odds ratio 1.74, 95% confidence interval 1.06-2.86, P < .5). Other variables were not predictive of outcome in multivariate analysis.

DISCUSSION

Here, we report a retrospective longitudinal cohort study of 241 TLE patients who underwent temporal lobectomy for medically refractory TLE, and analyze seizure types and frequencies before and after surgery. After surgery, 72.2% of patients achieved an Engel class I outcome—58.5% completely seizure-free (Engel IA) and 13.7% free of disabling seizures (Engel IB-D). As in previous studies by Engel, Spencer, Wiebe, and others, all individuals without residual disabling seizures (Engel IA-D) were considered to have a very favorable outcome. ^{4,26,27} However, the present study is the first, to our knowledge, to specifically examine the rates of consciousness-sparing and consciousness-impairing seizures after temporal lobectomy. We found that, although the number of patients experiencing consciousness-sparing SPSs decreased by only 19% after surgery, the number of individuals having consciousness-impairing CPSs and GTCSs diminished significantly more by 70% and 68%, respectively. SPS was the predominant seizure type in only 19.1% of patients preoperatively, but was the predominant seizure type in significantly more (37.0%) individuals with persistent postoperative seizures. The frequency of seizures in patients who continued to seize after surgery decreased by 70% overall, with the largest decreases seen among consciousness-impairing seizure types. A very favorable

FIGURE. Seizure types and frequencies before and after temporal lobectomy for TLE. A, number of patients with SPSs, CPSs, GTCSs, or any seizures preoperatively and postoperatively. Although the number of patients experiencing SPSs decreased by only 19% after surgery, the number of individuals having CPSs and GTCSs diminished by 70% and 68%, respectively ($\chi^2 = 16.9$, P < .001). The number of patients with "any" seizure does not equal the sum individual seizure types, because some patients experience more than 1 seizure type. B, proportions of individuals with each predominant (ie, most common) seizure type before and after surgery, among patients with persistent postoperative seizures. Although SPS was the predominant seizure type in only 19.1% of all patients before surgery, it was more frequently (37.0%) the predominant seizure type among patients still having seizures after surgery (χ^2 = 11.4, P < .01). C, D, seizure frequencies are shown preoperatively and postoperatively, among 100 patients who did have seizures after surgery (C), and 141 patients who achieved complete seizure freedom after surgery (D). Compared with preoperative baseline, patients with continued seizures after lobectomy experienced SPSs 65% less frequently (unpaired Student t = 2.9, P < .01), CPSs 73% less often (t = 2.4, P = .02), and GTCSs 78% less often (t = 1.3, P = .19), leading to an statistically significant 70% decrease in overall seizure frequency (t = 3.0, P < .01). Preoperative baseline seizure rates did not differ significantly between patients who ultimately did achieve seizure freedom (**D**) vs those who did not (**C**) (P > .15 for all comparisons). Data (**C**, **D**) are mean ± SEM number of seizures per week. CPS, complex-partial seizure; GTCS, generalized tonic-clonic seizure; SPS, simple partial seizure; TLE, temporal lobe epilepsy; SEM, standard error of the mean.

TABLE 2. Patient Seizure Outcomes^a More Favorable Less Favorable **Continuous Variables** Seizure Outcome^b Seizure Outcome^c P Value mean \pm SEM mean \pm SEM t test Age at surgery Years 34.9 ± 1.0 34.0 ± 1.6 .61 20.1 ± 1.0 Duration of epilepsy 20.1 ± 1.6 Years .99

Categorical Variables		% Patients by Row	% Patients by Row	χ^2
Sex	Male	72.8	27.2	.89
	Female	71.7	28.3	
Handedness	Right	72.9	27.1	.50
	Left	66.7	33.3	
Surgery side	Right	72.3	27.7	.99
	Left	72.1	27.9	
Number of epilepsy risk factors	0	74.3	25.7	.71
	1	68.3	31.7	
	≥2	71.0	29.0	
Previous resection	No	73.2	26.8	.20
	Yes	53.8	46.2	
Generalized seizures	No	77.8	22.2	<.01 ^d
	Yes	59.5	40.5	
MRI	Abnormal	76.0	24.0	.01 ^d
	Normal	47.4	52.6	
Ictal EEG ^e	Localizing	74.2	25.8	.08
	Nonlocalizing	59.0	41.0	
Implanted electrodes	Used	66.0	34.0	.26
	Not used	75.5	24.5	
Intraoperative ECoG	Used	69.1	30.9	.59
	Not used	73.8	26.2	
Pathology	MTS	71.7	28.3	.25
	Normal/gliosis only	64.4	35.6	
	Tumor	85.7	14.3	
	Cortical dysplasia	62.5	37.5	
	Other	75.0	25.5	

^aEEG, electroencephalography; ECoG, electrocorticography; MRI, magnetic resonance imaging; MTS, mesial temporal sclerosis; SEM, standard error of the mean.

seizure outcome—defined as seizure freedom or only residual nondisabling seizures—was predicted by a lack of generalized seizures preoperatively, consistent with previous studies. ²⁸⁻³⁰ These results suggest that some TLE patients who "fail" temporal lobectomy and continue to have seizures may nonetheless receive some benefit from surgery, particularly in the form of fewer consciousness-impairing seizures, which have been associated with increased morbidity compared with consciousness-sparing seizures.

Clinical and Mechanistic Differences Between Consciousness-Sparing and Consciousness-Impairing Seizures

Although it is well recognized that GTCSs, or convulsions, are associated with increased morbidity compared with partial seizures, 11 there are also important severity distinctions between

consciousness-impairing (CPSs) and consciousness-sparing (SPSs) partial seizures. ¹⁰ Consciousness-impairing seizures are associated with increased morbidity, including motor vehicle accidents and drownings, poor work and school performance, and social stigmatization resulting in a major negative impact on patient quality of life. ¹⁶⁻²⁰ Indeed, translational and basic studies have uncovered important differences in how SPSs vs CPSs impact brain networks. In intracranial EEG studies of TLE patients, CPSs are associated with abnormal slow-wave activity in frontoparietal association cortex resembling rhythms seen in sleep or coma, as well as bilateral temporal lobe fast activity, whereas, in SPSs, ictal electrographic abnormalities are generally confined to the ipsilateral temporal lobe. ^{21,31} On single positron emission computed tomography, decreased frontoparietal cerebral blood flow is noted during ictal neocortical slow activity in CPSs, but is not seen during SPSs. ²²

^bSeizure-free or only rare consciousness-sparing seizures (Engel IA-D).

^cPersistent consciousness-impairing seizures (Engel II-IV).

^dStatistically significant value (P < .05).

elctal EEG represents the ictal portion of long-term scalp video-EEG monitoring.

Rodent studies have also investigated potential network effects of temporal lobe seizures, finding that ictal increases in neuronal activity in limbic structures leads to decreased activity in the frontoparietal neocortex, but that a surgical fornix lesion prevents the distal cortical effects of limbic seizures—essentially turning a "CPS" into a "SPS."^{32,33} In humans with TLE, recurrent deleterious effects of seizures on the neocortex may lead to gray matter atrophy and hypometabolism between seizures, ^{34,35} and may be related to neuropsychological sequelae and chronic cognitive impairments frequently experienced by TLE patients. ^{3,36,37}

The Ultimate Goal of Epilepsy Surgery Is Complete Seizure Freedom

Although the present study suggests that certain TLE patients with postoperative seizures may nonetheless receive some benefit from surgery, this is not an entirely novel idea, and it does not change the primary goal of resective epilepsy surgery: complete seizure freedom. The Engel outcome scale and comparable multitiered classification schemes have long suggested that postoperative seizure outcomes are not dichotomous. Nevertheless, the present study is the first, to our knowledge, to specifically emphasize the presence and rates of consciousness-sparing vs consciousness-impairing seizures in TLE patients who "fail" temporal lobectomy. Next, although a decrease in the frequency of consciousness-impairing seizures may not represent a complete treatment failure, it is also not a complete success. Seizure freedom is the single most important predictor of quality of life after epilepsy surgery, leading to improved cognitive and physical function and overall satisfaction with treatment. 8,9 Furthermore, while resective epilepsy surgery is relatively safe, it is still associated with 2% significant morbidity and 0.24% total surgical mortality—risks that must be weighed against the expected surgical benefit. 5,38,39 Complete seizure freedom without perioperative adverse events must remain the objective of each resective procedure for focal epilepsy.

Study Limitations

There are several notable limitations to the present study. First, although data integrity was carefully scrutinized, this is a retrospective investigation, so the potential for bias is an important concern. Next, a major focus of the study involves rates of consciousnesssparing vs consciousness-impairing seizures before and after surgery, and, although previous studies have suggested differences between these seizure types with regard to patient safety, quality of life, and neurobiological mechanisms, these factors were not measured here. Other important outcome considerations in epilepsy surgery—such as freedom from AEDs, neuropsychological outcomes, and perioperative morbidity—were also not studied here, given the limited scope of this study. A more comprehensive and reliable assessment of the impact of temporal lobectomy on seizure type and frequency will require prospective study. Finally, although the present study is a descriptive investigation of seizure types in "failed" epilepsy surgery, future work should further analyze the reasons for surgical failures, including the role of preoperative functional diagnostic studies.

CONCLUSION

Temporal lobectomy is an effective treatment for intractable TLE, and among 260 patients in the present surgical series, 72% achieved freedom from disabling seizures after surgery. Although control of the most disabling and dangerous seizure types is common after temporal lobectomy, patients should be counseled that residual SPSs are not uncommon postoperatively. Our group has rarely performed surgery on patients with only SPSs, for whom the likelihood of complete seizure control may be modest. Overall, complete seizure freedom remains the ultimate goal in the medical and surgical treatment of patients who have epilepsy.

Disclosure

The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

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CME Questions:

- 1. When counseling a patient regarding temporal lobectomy for temporal lobe epilepsy, what is the most consistent and important predictor of a very favorable outcome after surgery?
 - A. Absence of generalized seizures preoperatively
 - B. Age < 50 years
 - C. Male gender
 - D. Confirmation of laterality based on invasive monitoring
 - E. Duration of epilepsy > 20 years
- Approximately what percentage of patients experience favorable outcomes (Engel Class I) 3-5 years after temporal lobectomy for temporal lobe epilepsy?
 - A. 30%
 - B. 50%
 - C. 70%
 - D. 90%
 - E. 10%
- 3. Patients who continue to seize after temporal lobectomy for temporal lobe epilepsy still experience an overall 70% reduction in seizure frequency. What type of seizure is reported to have larger reductions in frequency in response to temporal lobectomy in this patient population?
 - A. Consciousness impairing seizures
 - B. Consciousness sparing seizures
 - C. Seizures with aura
 - D. Seizures without aura
 - E. Focal seizures