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Suicide Outcomes After Resective Epilepsy Surgery

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Abstract

People with epilepsy have a higher risk for suicide than people without epilepsy. The relationship between seizure control and suicide is controversial. A standardized protocol to record history, diagnostic testing, and neuropsychiatric assessments was administered. The Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BDA) were administered presurgically and yearly for up to five years. Of the 396 enrolled, 4/27 deaths were attributed to suicide. The standardized mortality ratio, compared to suicides in the U.S. population and adjusted for age and gender, was 13.3 (95% CI=3.6, 34.0). Only one patient had a BDI score suggestive of severe depression (BDI=33), one had depressive symptoms that do not the meet the depressive range (BDI=7), while the other two reported no depressive symptoms. Two of the patients reported moderate to severe anxiety symptoms (BDI = 17 and 21, respectively). Suicide may occur after epilepsy surgery even when patients report excellent seizure control.

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Keywords

Epilepsy; Depression; Suicide; Neurosurgery; Mortality

Introduction

People with epilepsy (PWE) have a 3–25 fold higher risk for suicide than people without epilepsy.[1] The prevalence rate of suicide and suicide attempts in PWE ranges from 5–14.3% and in the general population from 1–4.6%. Suicide accounts for approximately 11% of the mortality rate in PWE.[2] A lifetime history of a mood disorder is the most significant risk factor for suicidality; 90–95% of PWE carry at least one Axis I diagnosis at the time of the suicide attempt.[3] Anti-epileptic drugs (AEDs) are a risk factor for suicide[4], but their role is controversial.

The relationship between seizure control and suicide is also controversial[4]. Hesdorffer et al found that people with a history of suicide and depression are more likely to develop seizures.[5] Small case series suggest that good seizure control is associated with increased depression and suicide rates, consistent with the forced normalization theory[6].

Long-term post surgical series found that patients who committed suicide had good or poor seizure control.[6,7,8] We studied a prospectively collected cohort of epilepsy surgery patients and describe the characteristics of those who committed suicide.

Methods

Data come from the prospective Multicenter Study of epilepsy; methods were described previously.[9] A total of 396 subjects were enrolled between 1996 and 2001 from six surgical centers to evaluate outcomes of resective epilepsy surgery.

A standardized protocol to record history, neurological evaluation, MRI, video-EEG monitoring, and neuropsychiatric assessments was administered. The Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI) were administered presurgically, then at three months post-surgery, and followed by yearly intervals up to five years. The BDI and BAI were validated in PWE and a score of >=16 correlates with moderate to major depression and anxiety disorders, respectively.[10] The World Health Organization Composite International Diagnostic Interview (CIDI) was also administered at baseline, presurgically, and two years after surgery. Quality of life was measured yearly using the QOLIE-89. At each interval patients ranked their functional expectations, activity level, and amount of driving. Postoperative complications were recorded by the patient's subjective report and by a research associate, who also reviewed the medical record. Cause of mortality was reported during interval follow up periods. Deaths were further ascertained by phone interviews with subjects' significant others, social security death index interactive search, review of medical examiner and obituaries.

To compare our suicide mortality rate to that in the U.S. population, we obtained information about suicide rates from the U.S. Center for Disease Control website[11]. We restricted the information to US population between the ages of 15 and 74, the same age range represented by patients in the surgery cohort. Because suicide rates in the US population were relatively stable across this age range and because we had only four suicides in our cohort, we calculated the overall suicide rate in the US population age 15–74 and contrasted that to the suicide rate observed in our cohort, adjusting for gender differences. Person-time was calculated as the years since date of surgery to date of last contact. The SMR was calculated as the observed number of suicides divided by the

expected number based on gender-specific years of follow-up and US gender-specific suicide rates.

Results

Postoperative outcome data were available for 316 patients after five years (See Table 1). In the US population, the yearly suicide rate in the 15–74 year age range was 1.3/10,000 deaths per year. In our cohort, we observed 4 suicides during the course of 2296 person-years of follow-up for a rate of 17.4/10,000 deaths per year. The sex adjusted standardized mortality ratio (SMR) was thus 13.3 (95% CI=3.6, 34.0). All four deaths occurred when the patient was seizure free >= one year based on last visit. Two patients were females; ages ranged from 33–45 years. One patient had a BDI score (33) consistent with severe depression, one reported depressive symptoms but the BDI score (7) was below depressive disorder range; two reported no depressive symptoms in the interviews before suicides. Two patients reported moderate to severe anxiety symptoms (BAI = 17 and 21), one had no depressive symptoms on the BDI. The CIDI assessments were not done at baseline and at two-year follow up for one patient and were normal at baseline and two- year follow up for another patient. One patient had severe panic disorder at baseline and developed a Major Depressive Disorder with Somatization (all post-surgical BDIs were “0”). The other patient had a Situational Phobia at baseline but did not have a CIDI completed at two-year follow up. All patients were taking AEDs at the visit prior to their death. Patient expectations, level of activity, and postoperative complications are detailed in Table 1.

Conclusion

Our subjects died of suicide at a significantly higher rate than the general U.S. population (SMR=13.3). In a meta-analysis, Bell et al have calculated that people with epilepsy with temporal lobe resection have a higher mortality rate due to suicide than non-surgical cases (SMR=13.9 vs 3.3).[12] Salanova et al demonstrated that people who continued to have seizures after surgery had a SMR of 7.4 in contrast to those who were seizure free post-surgery (SMR=1.7); 2/11 deaths were due to suicide.[13] Likewise, Hennessy et al. demonstrated that overall post surgical patients had higher mortality rate compared to the general population (SMR=4.5).[8] One of their 20 deaths were due to suicide in a subject who had post-surgical depression but was seizure free. Nilsson et al reported a similar post surgical mortality rate (SMR=4.9) but no difference based on seizure outcome and no suicides.[14]

All of our patients who committed suicide reported good seizure control prior to their deaths and all reported that surgery had a strong or very positive impact on their lives and would “definitely” have surgery again given their experience. Details regarding the circumstances leading to the suicides were unavailable. We do not know if life events, breakthrough seizures, or other confounding psychosocial circumstances precipitated suicides. These cases suggest that good seizure control after a successful surgical resection does not eliminate the risk of suicide.

While we are unable to determine the cause of suicide in our subjects, we may speculate that neurobiological changes due to direct injury of limbic networks or shifts in neurotransmitter networks post-surgery may have contributed to suicidality. Frontal and temporal lobe circuits and shifts in serotonergic activity, have been implicated in suicidal behavior in both people with and without epilepsy.[15] Some anti-epileptic drugs have been shown to be depressogenic; however, our subjects were not taking those medications.[4] Interestingly, two of the subjects were initially using lamotrigine, well known for its anti-depressant affect[4], prior to surgery but were discontinued after surgery.

The "Burden of Normality" may contribute to why patients with good seizure control committed suicide[16]. Epilepsy often provides social and emotional protection from day to day demands[17]. However, a surgical cure eliminates the "excuse" that seizures impair psychosocial performance. The burden of normality can includes psychological, behavioral, affective, and sociological features[16]. Psychologically, for example, patients may hold cognitive beliefs that they need to prove how they are "normal" and create unreasonable expectations. They may grieve for the lost opportunities they may have had if the surgery was done earlier. Behaviorally, seizure free patients may try too hard to make up for time lost, increasing their stress. Conversely, they may shirk or avoid productive activity for fear of ending the sick role. They may replace seizures with psychosomatic symptoms and non-epileptic seizures. Affective dysregulation has been described post-surgically which may lead to new mood, anxiety, or psychotic symptoms. Sociologically, the burden of normality may dramatically disrupt family dynamics, which developed mechanisms to care for the chronically ill patient, and may lead to disappointment if expected vocational, educational, and personal ambitions are not achieved. The factors hypothesized to contribute to the burden of normality were not captured in this study.

In our study the quality of life measures remained stable, suggesting there were no major stressors preceding the suicide. However, while the quality of life measures reflect some level of general health, physical, psychological, social, and cognitive function, they do not specifically measure patient's sense of self worth, discrepancy in their personal expectations and performance, or family dynamics.

One of the limitations of this data is that prior suicide attempts and ideation before surgery was not assessed in these patients and may have added additional risks. Another limitation is that the BDI was taken on a yearly basis and the BDI is designed to report a patient's subjective mood state of two-week intervals. Since the exact dates of the suicides are not available, and it is highly unlikely that the suicides all happened within two weeks of when the BDI was administered, the actual state of the patients at the time of the suicide is unknown. In the clinical setting most patients who are seizure free will likely be followed in six month or one year intervals, therefore, the administration of the BDI simulated how depression would be monitored in the natural clinical setting. Of particular concern, one patient denied any depressive symptoms on the BDI while his CIDI suggested that he developed a Major Depressive Disorder. Furthermore, while much of the epilepsy and suicide literature focuses on depressive symptoms the role of anxiety as a risk factor for suicide is well described in the broader psychiatric literature, and in fact was present in one of the patients.

Future research in epilepsy surgical outcomes should continue to include psychosocial variables such as psychiatric state and trait, quality of life, as well as adjustment to normalcy measures. The risk of suicide in epilepsy is higher than in the general population. Our findings highlight the fact that treatment and control of the seizures alone may not be enough to mitigate this risk. Even successfully treated patients should be monitored, supported, and transitioned into wellness[18].

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Table 1

Demographic characteristics, Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI) scores, quality of life measures (QOL), and seizure control in the four patient who died of suicide.

Demographics	**A**	**B**	**C**	**D**	**Work & Socialization**	**A**	**B**	**C**	**D**
Age at Surgery	45	44	35	33	Change in Employment	No	No	Yes, part time work,	No
Sex	M	F	F	M	Change in Education	No	No	No	No
Ethnicity	White	White	White	White	Enrolled in Educational Program	No	No	No	No
Education (years)	18	14	12	22	Change in Marital Status	No	No	No	No
					Driven a Car	No	No	No	Yes, daily
BDI/BAI Scores					Physical activity	Yes	Yes	Yes	No
Presurgical	1/21	25/22	6/10	0/0	Attends group meetings	No	No	No	Yes
3 Months	0/0	27/15	7/1	0/0	Religious services	Yes	Yes	No	Yes
12 Month	0/0	33/17	-	1/0	Volunteers	No	Yes	No	Yes
24 Months	-	-	-	0/1	Take care of children	No	Yes	Yes	No
36 Months	-	-	-	0/0					
60 Months	-	-	-	0/21					
QOL Scores									
Baseline	33.4	29.8	43.7	59.5	**AED**				
3 Months	48.2	37.8	49.7	56.9	Initial	LTG, CBZ	PHT	CBZ	LTG, CBX
12 Months	70.1	31.3	-	60.3	Tapered Off	CBZ (failed)			LTG, CBX
24 Months	-	-	-	62.4	New AED	PHT, LZP			CBX
36 Months	67.2	-	-	62.5					
48 Months	-	-	-	62.1	**Reported Complications**				
60 Months	-	-	-	61.5	Subjective Report	None	hemiparesisunsteadiness, memory problems, personality changes, insomnia, anxiety, nausea, vomiting, and/or GI complaints	word finding problems, verbal/visual memory problems, depressionpersonality change, anxiety, insomnia	None
Seizure Days									
Baseline	15	8	59	8					
6 Months	23	0	0	0					
12 Months	6	0	-	0	**Perception of surgery**				

Demographics	A	B	C	D	Work & Socialization	A	B	C	D
24 Months	-	-	-	0	Impact it had on your life	Very strong positive impact	Very strong positive impact	Strong positive impact	Strong positive impact
36 Months	-	-	-	0	Would you have surgery again?	Yes, definitely	Yes, definitely	Yes, definitely	Yes, definitely
48 Months	0	0	0	0					
60 Months	-	-	-	0					