Original Research

Factors Influencing Delay in Epilepsy Surgery: A Retrospective Data Review for a Tertiary Referral Center

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Medically intractable focal epilepsy affects a third of patients with seizures which are potentially surgically remediable. Several factors have been suggested for the reasons of the delays in epilepsy surgery. Nationally, the average time to surgery after onset of seizures is 20 years. We analyzed the characteristics of population of patients in Western New York who underwent surgery for refractory epilepsy, the time duration between onset of epilepsy and surgery, and the factors influencing the time duration, in order to determine whether there is any difference between the data from Western New York and all states in United States of America. Retrospective chart review of 51 patients was performed on the patients diagnosed with refractory epilepsy from 2003-2014 who underwent surgery at our center. Demographic Data such age, gender, ethnicity, insurance information, seizure severity, number of medications, EEG results, MRI lesions, and time to surgery were collected. Linear regression forward model was used for analysis with significance value set at 0.05. Mean waiting time to surgery at our center was shorter (13.5 versus 20 years) compared to the other centers in the United States of America. Eighty-one% (37) of the patients were diagnosed with lesions on MRI, of which 13% (6) were tumors. Mean waiting time of patients with a lesion was 13.4 years versus 15.5 years for patients without a lesion. Mean time for pediatric patients was 4.5 years and while for an adult patient was 21 years. When linear regression forward model was applied, a shorter time to surgery was associated with pediatric patients with B = 11.81 (2.42, 21.2), p-value = 0.016. Our study suggests that pediatric patients underwent surgeries earlier compared to adult population, which may be due to earlier identification by the local pediatric neurologists. Further research with bigger sample size is needed to probe the factors influencing the time duration between onset of epilepsy and candidacy of epilepsy surgery.

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Key Words: *epilepsy surgery, refractory epilepsy, delay*

INTRODUCTION

Epilepsy is one of the commonest neurologic diseases, affecting 1% of the population. It is established that 20-30% of patients with chronic seizures are not adequately controlled by medications.[1-4] About three fourths of the cost of epilepsy in the United States is spent on this subset of epilepsy population.[5] Epilepsy surgery has been considered the standard of care [1,3] in this situation. A single Class I study and 24 Class IV studies indicate that the benefits of anteromesial temporal lobe resection for disabling complex partial seizures is greater than continued treatment with antiepileptic drugs, and the risks are at least comparable. For patients who are compromised by such seizures, referral to an epilepsy surgery center should be strongly considered.[6] However, surgery for epilepsy is underutilized and it is believed that physicians fail to refer patients or refer them too late to an epilepsy referral center.[3,7-9] In addition to clinical and diagnostic variables playing a role in clinical decision making for epilepsy surgery, Social factors have also been identified as key drivers of epilepsy care, outcomes, and disparities, but there is a limited understanding of what these factors are and how they translate into disparities.[10]

We herein describe the results of epilepsy surgery at a single referral epilepsy program, and examine the referral patterns and time frames to determine how and when in the course of their illness patients arrive at a referral epilepsy center, reached medical intractability and underwent surgery. We then discuss possible ways to improve accessibility of patients to epilepsy surgery.

METHODS

Cohorts and Protocols: Our patient cohort were consecutive patients who underwent epilepsy neurosurgery involving

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resections at University at Buffalo's Women's and Children's Hospital of Buffalo from January 1st, 2004 to December 31st, 2013. A total of 51 epilepsy surgeries took place during this time. Excluded were the patients who had a craniotomy without cortical resection (biopsy alone), Diagnostic intracranial electrode placements or patients who had Vagus Nerve Stimulators (VNS) placed.

The local institutional review board approved the study and HIPAA regulations were followed. The study did not require informed consent due to it being a retrospective chart review.

Study definitions: According to the International league against Epilepsy (ILAE) definition, Medically intractable Epilepsy/Drug Resistant Epilepsy was defined as failure of adequate trials of two tolerated, appropriately chosen, and used antiepileptic drug schedules (whether as mono therapy or in combination) to achieve sustained seizure freedom.[11] Most of the patients had reached medical intractability by the time the patients were referred to our center.

Pediatric patients were considered those patients who were less than 18 years of age at the time of referral to our epilepsy monitoring center at Women and Children's Hospital of Buffalo.

Pre-surgical Evaluation and Data collection: The core clinical pre-surgical evaluation included history and neurological examination, inter-ictal and ictal video EEG recordings, brain MRI, PET or SPECT scan, and when necessary, neuropsychological assessments and intracarotid amobarbital injections (Wada test). At surgery, intraoperative electrode placement was performed to identify abnormal regions of persistent background slowing and frequent interictal epileptiform discharges mapped relative to the zone of cortical abnormality and imaged lesion if necessary.

Demographic information, age at the onset of seizures, gender, ethnicity, insurance information, age at the time of diagnosis of intractable epilepsy were obtained. Nature of the lesion, presence of an intracranial tumor, seizure focus, type of surgery, number of medications and other comorbidities were also recorded using the electronic medical record as well as charts from the Epilepsy Monitoring Unit. The severity of epilepsy was measured by using the modified Engel classification of seizure outcomes among the patients.[12] Epilepsy severity scale was further categorized into being seizure free, mild, moderate or severe groups depending on the frequency of seizures the patients had.[13] Surgery onset to seizure time in years was also obtained, which was used with the patients' clinical and demographic characteristics to analyze the reasons for delays.

Data Analysis: Statistical analysis for each outcome variable was analyzed using SPSS software (V.22, IBM Software, Chicago, Illinois, USA). A multistage analytic approach was used to assess the associations between dependent and independent variables. In the first step, univariate associations were determined. The associations between mean age of seizure onset with surgery time in years and dichotomous variables were determined using independent t-tests. In addition, association between mean surgery time in years and seizure severity scale was evaluated using analysis of variance (ANOVA). Additionally, a multiple linear regression analysis was conducted using a forward model approach to evaluate which of the independent variables could better explain the reasons for deferrals in epilepsy surgery. For statistical Analysis, the p-value was set at < 0.05 to reach statistical significance.

RESULTS

A total of 51 patients underwent craniotomy for possible epilepsy surgery. Four patients were excluded from analysis as the patients only had subdural electrode placements. A total of 47 patients were recorded for analysis. Females accounted for 52% of the cases while 48% were males. Our patient population constituted 82% Caucasian patients while the rest belonged to other ethnic backgrounds. Only 25% of the patients were on Medicaid at the time of evaluation. Mean age at seizure onset was 9.1 years. Mean age at the time of surgery was 23.3 ± 16.8 years. Average seizure onset to surgery time was 13.5 years. Temporal lobectomy was the most common epilepsy surgery among the patients accounting for 33 out of 47 patients. Among these patients, 36 patients had MRI findings positive for a lesion. Moreover, 7 out of these 36 patients had lesions that were consistent with a malignancy confirmed by pathology. There were 16 patients who were classified as having Intellectual Disability and 22 patients classified as having no intellectual disability whereas 9 patients had undetermined disability.

Mean time of deferrals in surgery was found to be statistically significantly shorter in pediatric patients as compared to adult patients with a mean time of 16.9 ± 3.23 years (independent t- test, p-value < 0.001). However, when mean time of deferrals in surgery was compared with gender, ethnicity, type of insurance, type of surgery, Seizure severity scale, MRI findings, EEG findings, nature of the lesion and intellectual disability, no significant difference was observed.

Furthermore, forward model linear regression analysis indicated a statistically significant association between shorter time delays in epilepsy surgery and being a pediatric patient, B = 11.81 (2.42, 21.2), p-value = 0.016.

DISCUSSION

The purpose of this study was to determine associations between the delays in epilepsy surgery at our center and demographic and clinical characteristics of the population. Statistically significant association was found only in pediatric patients where the mean time for epilepsy surgery was remarkably shortened in those cases. Moreover, the association was also established using regression analysis. The analysis suggests that the abovementioned results could account for only 19.4% of the variability in delays. Results from our data suggest a shorter time interval to surgery compared to the national average. Previous trends from studies at other comprehensive centers had an average time of 18 years.[14] The definitive reason for the shorter intervals

in timing for epilepsy surgery for pediatric patients is not precisely discernable from our data. It is important to note that we did not have a definitive time of diagnosed intractable epilepsy at the time of the referral for surgery. Some of the patients who had epilepsy surgery among our cohort were the patients who were inherent to the practice group at Women and Children's Hospital of Buffalo. Hence, it is possible that the shorter time intervals among the pediatric population was due to the closer surveillance by the pediatric neurologists and availability of services.

Table 1. Linear regression model evaluating statistically significant clinical variable.

	Standardized coefficient Beta	P - value	95% Confidence interval	
			Lower bound	Upper bound
Age group (adult vs pediatrics)	0.477	0.016	2.42	21.19

Table 2. Association of mean time intervals to surgery and demographic and clinical characteristics.

Characteristics		Mean time to surgery from seizure onset (years)	Sum (N)	p-value
Gender	*Male* *Female*	10.6 16.08	23 24	0.167
Ethnicity	*Caucasian Others*	13.2 15.29	38 9	0.708
Insurance	*Medicaid Others*	18.9 12.4	11 32	0.174
Type of Surgery *Temporal lobectomy* *Extratemporal surgery/lesionectomy*		 12.3 10	 33 14	0.590
Age Group	*Pediatric Adult*	4.5 21.4	23 24	0.000
MRI lesion	*Positive Negative*	13.4 14	36 11	0.86
Nature of lesion *Tumor* *Non tumorous*		 8 39	 8.2 14.3	0.358
Intellectual Disability *Yes* *No*		 15.6 9.8	 17 17	0.191
Seizure Severity Scale* *Seizure free* *Mild* *Moderate* *Severe*		 0 14.1 16.8 7.2	 0 9 24 10	0.184
No. of Anti-Epileptic Medications* *1* *2* *3* *4*		 1.2 15.3 13.6 7.8	 4 15 14 5	0.190

Several investigations have reported differences in the incidence of adult and pediatric epilepsy surgery and also have shown reduced interval times for pediatric patients.[14-16] However, due to the complexity of the disease and other factors working in concert, the magnitude of the association remains undetermined. In addition, the previous investigations had factors that had a stronger association with other demographic variables compared to the variable in light in the present study.[14,16] Moreover, the natural course of epilepsy suggests that some of the epilepsy syndromes shift towards regression spontaneously with age which could be another factor playing a role in the dichotomy of the timings of epilepsy surgery.

A proposed theory for the association between time delay in epilepsy surgery among pediatric and adult patients is the early identification by the pediatric neurologists at our academic center. The identification of drug resistant epilepsy and timely referral to a comprehensive epilepsy care center could lead to early treatment which would limit the permanent damage caused by epilepsy and would improve quality of life. However, this would also mandate that the community neurologists including adult neurologists be made cognizant of the recognition patterns of the disease. Surveillance studies should be carried out to ascertain physicians' concept of epilepsy surgery and the attitudes of practice by neurologists.[17] A better understanding of medical

professionals on the subject will lead to earlier referrals and in turn will impact patient outcomes.

In conclusion, the data from our center and other centers across United States and other developed countries suggests that there has not been a change in the incidence of epilepsy surgeries or a change towards reducing time intervals between seizure onset and surgery times over the past 10 years.[14,18] If this were indeed the case, it would have serious implications for epilepsy surgery programs. It would not only need a change to address the attitudes of the physicians and patient misconceptions about epilepsy surgery but it would also need to bring about restructuring of the epilepsy programs.

CONFLICT OF INTEREST

The authors have no conflict of interest to disclose.

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