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Research Paper

Sociodemographic Factors in Pediatric Epilepsy Surgery

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ABSTRACT

Background: Despite documented efficacy of surgical treatment in carefully selected patients, surgery is delayed and/or underutilized in both adult and children with focal onset epilepsy. The reasons for surgical delay are often assumed or theorized, and studies have predominantly targeted the adult population. To focus on a more targeted pediatric population and to determine identifiable reasons for intervention, this study aimed to investigate time to epilepsy surgery among pediatric patients with medically intractable epilepsy associated with focal cortical dysplasia and to identify sociodemographic and clinical associations in time to epilepsy surgery.

Methods: We reviewed 96 consecutive pediatric patients who underwent surgery for medically intractable epilepsy with a diagnosis of focal cortical dysplasia. Descriptive statistics, univariate and multivariate analyses were conducted to study the association of sociodemographic variables of patients with focal cortical dysplasia and time to epilepsy surgery and postoperative seizure control.

Results: We identified that non-white patients on average had a longer duration of epilepsy before surgery and traveled shorter distances for care. Non-white patients were more likely to have government-funded insurance. Patients who traveled the shortest distance to the surgical center underwent epilepsy surgery at an older age.

Conclusions: Sociodemographic factors of travel distance, insurance, and race influenced time to epilepsy surgery for children with focal cortical dysplasia. Further research is warranted to target barriers in access to subspecialty care and develop ways to identify earlier the patients who may benefit from evaluation and deployment of surgical intervention.

Introduction

Epilepsy is a common neurological problem, affecting approximately 1% of the general population.[1,2] Although the majority of patients with epilepsy are managed well with antiseizure medication, approximately 20% to 30% of patients with chronic seizures are not adequately controlled with medications alone.[1-3] Medically intractable epilepsy is commonly defined as a failure of seizure control with adequate trials of two antiseizure drugs, either as monotherapy or in combination.[1,3] Mesial temporal lobe epilepsy is a common etiology of medically intractable epilepsy in adults and has an excellent rate of postsurgical seizure freedom.[2,4] This population has been extensively studied, and The American Academy of Neurology recommends surgery as the treatment of choice for medically intractable mesial temporal lobe epilepsy.[2,4-6] However, children with focal medically intractable epilepsy represent an entirely different population, with unique demographics and pathology and higher postsurgical seizure freedom than adults.[7]

Despite evidence of the efficacy of surgical resection, recent growth of epilepsy surgery centers, and improved surgical

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outcomes, there remains evidence of underutilization and of delays in epilepsy surgery for these patients.[2,4-6] Only an estimated 1% of patients with medically intractable epilepsy undergo surgery within two years of diagnosis, with a national average of 20 years from diagnosis to surgical treatment.[1,2,6] Delays in time to surgical intervention for suitable candidates may contribute to cognitive and psychosocial decline as a consequence of ongoing seizures and inadequate seizure control over time.[8-11] Limited studies of delays to epilepsy surgery in the pediatric population often use an umbrella approach, studying multiple pathologies. This approach maximizes cohort size and improves validity; however, it may amplify the confounding factors determining the time to surgery and the seizure outcome.[12]

We investigated the surgical utilization among children with focal cortical dysplasia (FCD). This study identifies a more discrete pathology, although with some variation in the site of origin and type of dysplasia. FCD is the most common cause of medically intractable epilepsy in pediatric patients and is characterized by malformations in cortical development and aberrant cortical cytoarchitecture.[13-16] FCD is a pathologic diagnosis, and lesions are classified as FCD I to III based on histopathological features, using the International League Against Epilepsy system.[17,18] Although FCD is confirmed by pathology, magnetic resonance imaging (MRI) is widely used as a diagnostic tool and for presurgical planning of dysplastic lesions. Radiological findings include blurring of the gray–white matter junction, cortical thickening, irregular gyral patterning, and subcortical hyperintensities.[19-22] FCD offers unique challenges for presurgical evaluation that may potentially contribute to delays in diagnosis and surgical management. Electroencephalographic findings often poorly localize to MRI-identified lesions, and MRI findings themselves are often subtle or difficult to detect.[19,20,23,24] Given the unique diagnostic challenges of FCD, this study aimed to characterize associations between sociodemographic factors and delays in epilepsy surgery in patients with FCD.

Methods

Patient population

We retrospectively reviewed 96 consecutive patients who underwent surgery from 2012 to 2016 at our tertiary academic hospital for medically intractable epilepsy and had MRI-identified lesional cases of FCD as well as those who had lesions not visible on MRI, but pathologically proven. Data collected from electronic medical record review included demographics, zip code, health insurance, seizure history, preoperative imaging, hospital course, and postoperative course. Travel distance to our medical center was calculated based on zip code. Patients were divided into three groups based on type of health insurance: private health insurance, government-funded health insurance, and no health insurance or uninsured. Post-surgical outcomes were evaluated with the Engel Epilepsy Surgery Outcome Scale at final postoperative follow-up that occurred at least at six months or later. Patients were divided into two groups based on Engel classification: favorable seizure control (Engel I and II) and poor seizure control (Engel III and IV). The continuous variables, distance traveled between home zip code and medical center and age at surgery, were grouped into quartiles for seizure outcome classification. This study was approved by the Institutional Review Board of the Baylor College of Medicine.

Statistical analysis

Fischer's exact and chi-square tests were used to analyze the effect of individual sociodemographic and clinical parameters on postoperative seizure outcome. One-way ANOVA and unpaired *t* tests were used to analyze differences in clinical and sociodemographic variables based on race, health insurance, distance traveled, and anatomical location of cortical dysplasia lesion. Logistic regression was performed for multivariate analysis of predictors of postoperative seizure control. Statistical analysis was performed using Graphpad Prism version 7 (GraphPad Software, La Jolla, CA, USA) and SPSS software (IBM, Armonk, NY, USA). The significance level was set at 0.05.

Results

Epilepsy surgeries

From 2012 to 2016, a total of 208 patients underwent epilepsy surgery at our institution. The age at surgery ranged from one month to 22 years (median = 12.0 years, S.D. = 5.83 years). Of 208 patients 59 had temporal lobe epilepsy, and age at surgery ranged from six months to 22 years (median = 11.0 years, S.D. = 6.06 years). Of the 208 patients 149 had an extratemporal site of epilepsy and age at surgery ranged from one month to 21 years (median = 10.5 years, S.D. = 5.86 years). In this same time frame, 96 of 208 patients had surgery for FCD; two international patients were excluded for incomplete data, bringing the total FCD cohort for analysis to 94 patients.

Patient population

Of the 94 patients with surgery for FCD, 54 were male and 40 were female. Age at seizure onset ranged from one month to 18 years (median = 3.0 years), and age at surgery ranged from eight months to 22 years (median = 12.0 years). The mean duration of post-operative follow-up was 24 months and ranged from six months to five years. Of the 94 patients 58 underwent a neuropsychologic evaluation with intelligence quotient evaluated by Differential Ability Scales (DAS-II), Wechsler Intelligence Test for Children (WISC-V), Wechsler Adult Intelligence Scale (WAIS-IV), Wechsler Preschool and Primary Scale of Intelligence (WPPSI-II), or Mullen's Scale of Early Learning. Two nonverbal patients were evaluated with the Leiter International Performance Scale, Third Edition. Full-Scale IQ test results ranged from 40 to 120 (mean = 83). The duration of epilepsy before surgery ranged from one month to 21 years (median = 5.0 years). Forty-nine patients had predominantly focal seizures without spread, and 45 patients had predominantly focal to generalized tonic-clonic seizures (FGTC). Eight patients were white (32 Hispanic patients, 48 non-Hispanic patients), and 14 patients were racial minorities (black, Asian, Native Hawaiian/Pacific Islander, and multiracial). Seventy-four patients traveled from within the state of Texas, and 20 patients traveled from out of state; 73% patients had private health insurance, 21% had government-funded health insurance, and 5% were uninsured (Table 1).

Engel outcome

Univariate analysis demonstrated that gender, distance traveled, type of health insurance, age at surgery, and anatomical location did not have a significant effect on postoperative seizure control at six months or greater postoperative follow-up (Table 2). Multivariate analysis was performed on variables with $P < 0.25$ in univariate analysis. Multivariate analysis demonstrated that race, history of previous surgery, and number of preoperative medications were not strong predictors of Engel outcome.

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TABLE 1.
Characteristics of Patient Population

Age at surgery	
Range (mo)	8-264
Median (yr)	12.0
Seizure onset	
Range (mo)	1-216
Median (yr)	3.00
Epilepsy duration	
Range (mo)	1-252
Median (yr)	5.00
Number of preoperative medications	
Range	1-6
Median	2.00
Seizure type (%)	
FGTC	45 (48)
Focal	49 (52)
Gender (%)	
Male	54 (57)
Female	30 (32)
Race (%)	
White	
Non-Hispanic	48 (60)
Hispanic	32 (40)
Non-white	14 (15)
Distance traveled (%)	
In-state (median = 30.7 miles)	
Below median distance	37 (39)
Above median distance	37 (39)
Out-of-state (median = 619 miles)	20 (22)
Health insurance (%)	
Private	69 (73)
Government funded	20 (21)
Uninsured	5 (5)
Previous surgery (%)	
Yes	33 (35)
No	61 (65)
Anatomical location (%)	
Frontal	30 (32)
Temporal	47 (50)
Parietal	7 (7)
Occipital	2 (2)
Multilobar	8 (9)

Abbreviation:
FGTC = Predominantly focal to generalized tonic-clonic seizures

TABLE 2.
Univariate Analysis of Demographic and Clinical Factors for Surgical Outcomes at Postoperative Follow-Up

Variables	Engel Class		
	I/II (n = 68) n (%)	III/IV (n = 26) n (%)	*P* Value
Race			
White			
Non-Hispanic	34 (50)	14 (54)	0.23
Hispanic	26 (38)	6 (23)	
Non-white	8 (12)	6 (23)	
Gender			
Male	40 (59)	14 (54)	0.82
Female	28 (41)	12 (46)	
Age at surgery			
Quartile 1 (median = 4.00 yr)	19 (28)	4 (15)	0.26
Quartile 2 (median = 9.55 yr)	4 (21)	9 (35)	
Quartile 3 (mean = 15.0 yr)	20 (29)	5 (19)	
Quartile 4 (mean = 19.0 yr)	15 (22)	8 (31)	
Distance traveled			
In-state (median = 30.7 miles)			
Below median distance	28 (41)	9 (35)	0.69
Above median distance	27 (40)	10 (38)	
Out-of-state (median = 619 miles)	13 (19)	7 (27)	
Health insurance			
Private	50 (74)	19 (73)	0.90
Government funded	14 (21)	6 (23)	
Uninsured	4 (6)	1 (4)	
Anatomical location			
Temporal	34 (50)	13 (50)	>0.99
Extratemporal	34 (50)	13 (50)	
Seizure type			
FGTC	33 (49)	12 (46)	>0.99
Focal	35 (52)	14 (54)	
Number of preoperative medications			
<3 preoperative medications	42 (62)	12 (46)	0.24
≥3 preoperative medications	26 (38)	15 (54)	
Previous surgery			
Yes	21 (31)	12 (46)	0.23
No	47 (69)	14 (54)	

Abbreviation:
FGTC = Predominantly focal to generalized tonic-clonic seizures

Anatomical location

Forty-seven patients had cortical dysplasia in the temporal lobe, and 47 patients had dysplasia at an extratemporal site. The majority of extratemporal sites involved the frontal lobe (n = 30) rather than parietal (n = 7), occipital (n = 2), or multilobar (n = 8) involvement. An extratemporal location of dysplasia was associated with a higher number of preoperative antiseizure medications ($P = 0.02$), failed antiseizure medications ($P = 0.01$), and total postoperative medications at follow-up ($P = 0.01$). Dominant seizure type, onset, and epilepsy duration before surgery did not vary significantly based on anatomical location.

Race

Non-white patients had a longer duration of epilepsy before surgery ($P = 0.03$) and were less likely to be privately insured ($P = 0.001$). The median duration of epilepsy was 9.5 years in non-white patients compared with 4.0 years in non-Hispanic white patients and 6.6 years in Hispanic white patients (Table 3). Also, 64% non-white patients and 50% of Hispanic white patients were privately insured compared with 92% non-Hispanic white patients. Non-white and Hispanic white patients were more likely to travel the shortest distance for care ($P = 0.0003$) and had FGTC as the dominant seizure type ($P = 0.02$); 19% of non-Hispanic white patients traveled less than 31 miles for care compared with 63% of Hispanic white and 57% of non-white patients. Also, 63% Hispanic white patients and 64% non-white patients had more FGTC seizures compared with 33% non-Hispanic white patients. Total preoperative antiseizure medications, history of previous surgery, and total postoperative medications did not differ significantly between groups (Table 3).

Distance traveled to hospital

Patient zip codes were used to calculate the distance traveled to the hospital in miles. Patients were categorized into the travel groups: in-state and out-of-state. Patients who traveled from within the state of Texas were subdivided into above and below median distance traveled. Patients who traveled within the state of Texas had a median distance of 30.7 miles. Patients traveling from out of state had a median distance of 619 miles. Patients who traveled the shortest distance in state had surgery at an older age (median = 15.0 years, $P = 0.005$) and had a longer epilepsy duration before undergoing surgery (median = 9.00 years, $P = 0.01$). Furthermore, patients traveling in state had a higher rate of FGTC seizures compared with out-of-state patients ($P = 0.04$) (Table 4).

Discussion

This study provides an analysis of several important sociodemographic variables and their relationship with the clinical

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TABLE 3.
Comparison of Seizure and Demographic Characteristics by Race

Patient Characteristics	White		Non-White	*P* Value
	Non-Hispanic n = 48 n (%)	Hispanic n = 32 n (%)	n = 14 n (%)	
Sex				
Male	26 (54)	19 (59)	9 (64)	0.77
Female	22 (46)	13 (41)	5 (36)	
Distance traveled				
In-state (median = 30.7 miles)				0.0003
Below median distance	9 (19)	20 (63)	8 (57)	
Above median distance	23 (48)	11 (34)	3 (21)	
Out-of-state (median = 619 miles)	16 (33)	1 (3)	3 (21)	
Health insurance				
Private	44 (92)	16 (50)	9 (64)	0.001
Government funded	2 (4)	13 (41)	5 (36)	
Uninsured	2 (4)	3 (9)	0 (0)	
Seizure type				
FGTC	16 (33)	20 (63)	9 (64)	0.02
Focal	32 (67)	12 (38)	5 (36)	
Previous surgery				
Yes	17 (35)	10 (31)	6 (43)	0.75
No	31 (65)	22 (69)	8 (57)	
Anatomical location				
Temporal	21 (44)	21 (66)	5 (36)	0.08
Extratemporal	27 (56)	11 (34)	9 (64)	
Seizure onset				
Median, S.D. (yr)	4.00, 4.30	3.00, 3.28	3.00, 3.28	0.37
Age at surgery				
Median, S.D. (yr)	12.0, 6.00	11.0, 5.60	12.0,6.60	0.64
Epilepsy duration				
Median, S.D. (yr)	4.00, 4.22	6.58, 4.70	9.50, 6.50	0.03
Preoperative medications				
Median, S.D.	2.00, 1.00	2.00, 0.80	2.00, 1.15	0.05
Failed antiseizure medications				
Median ± S.D.	2.00, 1.82	2.00, 2.00	2.00, 2.85	0.83
Postoperative medications				
Median ± S.D.	2.00, 0.99	2.00, 0.95	2.00, 1.29	0.10

Abbreviation:
FGTC = Predominantly focal to generalized tonic-clonic seizures

TABLE 4.
Comparison of Seizure and Demographic Characteristics by Distance Traveled

Patient Characteristics	In State		Out-of-State	*P* Value
	Below Median n = 37 n (%)	Above Median n = 37 n (%)	n = 20 n (%)	
Gender				
Male	24 (65)	21 (57)	9 (45)	0.22
Female	13 (35)	16 (43)	11 (55)	
Seizure type				
FGTC	22 (59)	17 (46)	5 (25)	0.04
Focal	15 (40)	20 (54)	15 (75)	
Previous surgery				
Yes	13 (35)	12 (32)	8 (40)	0.61
No	24 (65)	25 (68)	12 (60)	
Seizure onset (yr)				
Median, S.D.	2.25, 4.05	4.00, 4.76	2.00, 3.27	0.16
Age at surgery (yr)				
Median, S.D.	15.0, 5.62	12.0, 6.20	6.00, 4.78	0.005
Epilepsy duration (yr)				
Median, S.D.	9.00, 5.31	5.00, 4.42	3.00, 4.12	0.01
Preoperative medications				
Median, S.D.	2.00, 0.89	2.00, 0.75	3.00, 1.32	0.01
Failed antiseizure medications				
Median, S.D.	2.00, 2.14	2.00, 1.61	3.00, 2.37	0.06
Postoperative medications				
Median, S.D.	2.00, 1.72	2.00, 1.37	3.00, 1.69	0.46

Abbreviation:
FGTC = Predominantly focal to generalized tonic-clonic seizures

profile of surgically managed patients with epilepsy with FCD. In this study, postoperative seizure control was favorable, with 72% patients with Engel class I and II outcomes, in keeping with seizure freedom rates ranging from 50% to 73% reported in the literature for FCD.[25-28] Duration of follow-up was at least six months with a range from six months to five years. The historical dogma that acute postoperative seizures are not predictive of long-term outcome has recently been called into question.[29-31] Although six months may seem to be a short follow-up period, seizures occurring before this time seem to be more predictive of outcome.[32,33] Although this may be the case, a short duration of follow-up for a number of patients is a limitation of the study. A potential barrier to longer duration of follow-up includes long distance from the surgical center.

Gender, distance traveled, anatomical location, age at surgery, and seizure type were not significant predictors of seizure outcomes. Our cohort of 94 patients did not demonstrate an impact of age at surgery or anatomic location of the lesion on outcome; some previous studies have reported that temporal resection is associated with better surgical outcomes, whereas other studies have not found significant differences.[14,28,34-36]

We found that patients of nonwhite race had a longer duration of epilepsy before receiving epilepsy surgery, were less likely to be privately insured, and traveled a shorter distance for care. Few studies have looked at the effect of race as an independent predictor of postsurgical seizure outcome.[5,37,38] In a cohort of 70 patients with mesial temporal sclerosis who underwent temporal lobectomy, African American patients were more likely than non-Hispanic Caucasian to experience seizure recurrence.[38] Previous studies have primarily focused on the utilization of surgery in the treatment of intractable epilepsy between racial groups. Among patients with intractable temporal lobe epilepsy, race independently predicts the likelihood of receiving temporal lobectomy.[37-39] Racial minorities, particularly African Americans, are less likely to undergo resective surgery as treatment for intractable epilepsy. The underutilization of surgical management of epilepsy may be in part attributable to negative historical experiences with the health care system.[8,33,37] Mistrust and fear of physicians as well as concerns of surgical risks among African American patients negatively influence their likelihood to undergo surgical treatment for epilepsy.[37-39] Physician-centered factors that may influence this disparity include communication skills, quality and quantity of information provided to the patient, and subtle racial bias.[39,40] Cultural perspectives, barriers to access to care, as well as physician-centered factors are potential factors that lengthen the time to surgery.

Local in-state travel was associated with an older age at surgery and longer duration of epilepsy before receiving epilepsy surgery. Patients traveling out of state were less likely to have FGTC seizures. Patients did not differ significantly in other clinical metrics, including number of failed antiseizure medications, history of previous surgery, and postoperative medications. These results suggest that the earlier time to surgery among those traveling further is not necessarily attributable to a higher clinical severity. Disparities in access to care or in level of patient advocacy of the patients' families may explain some of these observed differences.

Neither level of education nor number of communications from the families was measured. "Health care seeking behavior" is characterized in the literature, and described as whether, when, and from where care is sought. Health insurance type is implicated as a potential factor that influences health care-seeking behavior.[41-43] Presence of insurance coverage as well as the level of coverage are reported to be determinants of health care utilization.[41-43] In this study, non-white and Hispanic white patients were less likely to be privately insured, traveled the shortest

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distance to our center, and had longer duration of epilepsy before epilepsy surgery. Furthermore, patients with the shortest travel had an older age at surgery. The specific reasons for older age at surgery and longer duration of epilepsy in our local, Medicaid population are unclear and warrant further investigation. In day-to-day practical considerations, parents and caregivers bring children to appointments, imaging studies, and epilepsy monitoring unit stays; for those with employment obligations, these health care encounters may add up to a significant amount of time away from work. If these medical encounters occur frequently, financial security for some families may be at risk. For those families coming from out of state, our epilepsy surgery program coordinator may schedule all preoperative studies during a single visit, possibly inadvertently giving a time advantage to those traveling greater distances.

Limitations of this study include the known weaknesses of a retrospective review. In addition, the data originated from a single institution in an urban setting in Texas; the extent to which the results can be generalized is not clear. The 94-patient sample size is also limited, and further work with a larger experience is in progress. Socioeconomic data of family incomes is necessary to further evaluate financial barriers affecting access to care. Additional analysis of presurgical evaluation for our patient population would be warranted to further characterize surgical outcomes.

Future research efforts are warranted to investigate the risk factors for this possible delay in surgical treatment and issues in access to subspecialty epilepsy care. The duration of epilepsy before referral for epilepsy surgery reflects an opportunity for improvement in our region and local clinical practice, and also in overall health care delivery and policy. It is unclear if time to surgery impacts neurocognitive outcome or other variables unable to be addressed by this study. Future aims would include identification of patients who are surgical candidates earlier, with a shorter duration of epilepsy, to enable streamlined access to all who need diagnostics and treatments that may decrease burden of epilepsy to the child and the family.

Conclusion

This study demonstrates that sociodemographic factors may influence time to surgery for pediatric FCD. The study investigates a singular etiology of pediatric-intractable epilepsy to provide a focused analysis of factors affecting appropriate treatment of these patients. Public insurance coverage, non-white race, and geographic proximity to the hospital are significantly associated with longer duration of epilepsy before receiving epilepsy surgery treatment. Further research is warranted to target barriers in access to subspecialty care and develop programs to identify earlier the patients who may benefit from evaluation and deployment of surgical intervention.

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