The Effectiveness of Medical and Surgical Treatment for Children With Refractory Epilepsy

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BACKGROUND: Pediatric refractory epilepsy affects quality of life, clinical disability, and healthcare costs for patients and families.

OBJECTIVE: To show the impact of surgical treatment for pediatric epilepsy on healthcare utilization compared to medically treated pediatric epilepsy over 5 yr.

METHODS: The Pediatric Health Information System database was used to conduct a cohort study using 5 published algorithms. Refractory epilepsy patients treated with antiepileptic medications (AEDs) only or AEDs plus epilepsy surgery between 1/1/2008 and 12/31/2014 were included. Healthcare utilization following the index date at 2 and 5 yr including inpatient, emergency department (ED), and all epilepsy-related visits were evaluated. The propensity scores (PS) method was used to match surgically and medically treated patients. PS. SAS® 9.4 and Stata 14.0 were used for data management and statistical analysis.

RESULTS: A total of 2106 (17.1%) and 10186 (82.9%) were surgically and medically treated. A total of 4050 matched cases, 2025 per each treated group, were included. Compared to medically treated patients, utilization was reduced in the surgical group: at 2 and 5 yr postindex date, there was a reduction of 36% to 37% of inpatient visits and 47% to 50% of ED visits. The total number (inpatient, ED, ambulatory visits) of epilepsy-associated visits were reduced by 39% to 43% in the surgical group compared to the medically treated group. In those who had surgery, the average reduction in AEDs was 16% at 2 and 5 yr after treatment.

CONCLUSION: Patients with refractory epilepsy treated with surgery had significant reductions in healthcare utilization compared with patients treated only with medications.

KEY WORDS: Drug-resistant epilepsy, Effectiveness, Epilepsy surgery, Healthcare utilization, Pediatric epilepsy, Refractory epilepsy

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In 2015, it was estimated that 470 000 children in the United States (US) had epilepsy.[1] Among them, 20% to 30% were refractory to medical management.[2,3] Refractory epilepsy carries a significant impact on childhood development and quality of life for children and their caregivers.[4] Refractory epilepsy also confers substantial implications in healthcare use and costs. Children with refractory epilepsy also have higher medical care needs and consume substantially more healthcare resources, such as inpatient (IP) and emergency department (ED) visits, compared with children who have good seizure control with medications.[5]

Surgical resection has shown to be an effective treatment for appropriately selected cases of refractory epilepsy.[6-8] Patients with surgical treatment are reported to have 61% to 90% Engel class I or II outcomes,[9] with the rates of reported postoperative seizure freedom ranging from 66.7% and 77%.[10-12] Despite substantial evidence demonstrating effectiveness in seizure control with epilepsy surgery, few studies compare the outcomes and effectiveness between surgically and medically treated children with refractory epilepsy. Of the few studies which do so, results show that compared to medically

ABBREVIATIONS: AED, antiepileptic medication; **ED,** emergency department; **HU,** healthcare utilization; **ICD-9-CM,** International Classification of Diseases, Ninth Revision, Clinical Modification; **IP,** inpatient; **P-CCC,** pediatric complex chronic condition; **PHIS,** Pediatric Health Information System; **PS,** propensity scores; **SD,** standard deviation; **S-Diff,** standardized difference; **SUDEP,** sudden unexplained death in epilepsy; **VNS,** vagus nerve stimulation

treated patients, surgically treated patients tend to have increased overall survival and better quality of life.[12-14]

Objectives

There are no published healthcare utilization (HU) studies comparing medical vs surgical management in children with refractory epilepsy. The purpose of this study was to compare HU between medically and surgically treated children with refractory epilepsy in the US tertiary children's hospitals. We hypothesize that surgically managed children would more effectively reduce overall healthcare utilization, by reducing ED visits, IP visits and antiepileptic medications (AEDs) in the short term (2 yr) and over a sustained period (over 5 yr).

METHODS

Study Design, Setting, and Data Sources

Children's Hospital Association's Pediatric Health Information System (PHIS) data was used to conduct a retrospective cohort study. The database represents 13.3% of the national volume of all hospitalized pediatric patients in the US, excluding normal healthy newborns. Over 80% of these hospitals are Level 3 or Level 4 National Association of Epilepsy Centers that focus on childhood epilepsy treatment. The data contains IP, ED, ambulatory, and observation encounter level data from more than 40 children's hospitals since 2007. It also includes all charged items/services billed to the patient, pharmacy, imaging/radiology, lab, clinical, supplies, and other charges. Data elements in the database include patient demographics (age, sex, insurance, and race) as well as treatment details that allow us to examine variations in hospital utilization among subgroups receiving epilepsy treatment. All encounter-level data are de-identified. This study received exempt status from the university's Institutional Review Board. Waiver of patient/guardian consent was granted as the study was performed using de-identified, administrative database, patient data.

Study Cohort

The constructed study cohort (Figure 1) was initially queried in the PHIS Cohort Builder for children discharged between 1/1/2008 and 12/31/2014 with an IP hospitalization indicating an International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis of 345.XX (epilepsy and recurrent seizures) or 780.39 (other convulsions), age between 0 and 17 yr, and having completed records of IP, ED, and ambulatory services.

Children with epilepsy were then confirmed using the following published algorithms[6,15-18]: 1) at least 2 encounters with diagnosis code 345.XX on separate dates in any visit (including IP, ED, or ambulatory care); 2) at least 1 encounter with diagnosis code 345.XX and at least 1 separate encounter on a different date with diagnosis code 780.39; 3) a primary diagnosis code 345.XX and a therapeutic category code indicating AED; 4) at least 2 encounters with diagnosis code 780.39 and code(s) for AED; 5) an IP or ED visit with a primary diagnosis code 345.XX.[5]

Only confirmed epilepsy cases who had a primary diagnosis of 345.X1 indicated intractable epilepsy and had failed 2 AEDs or had an epilepsy surgery before 12/31/2014 were identified as refractory epilepsy and included in the final cohort. The first encounter date that met any of the above criteria was defined as the first date of refractory diagnosis. Patients who had a history of epilepsy (craniotomy) surgery before the study timeframe (1/1/2008) or a vagus nerve stimulation (VNS) implant, or expired at index admission were excluded.[5]

For the surgical group, the first admission date of the surgical IP visit within the study time frame was defined as the index date for the specific methodology purposes of study tracking. The first admission date of epilepsy IP services on or after the date of defined refractory epilepsy within the study time frame was defined as the index date for the medical group. Treatment information was extracted at least a year before the index date and was followed up 5 yr after the index date. The last stream of data was updated to 3/31/2018.

Interventions/Treatments

For surgically treated patients: cranial surgery was identified by ICD-9-CM procedure code: 1.52 (hemispherectomy), 1.53 (brain lobectomy), or 1.59 (partial brain lobectomy, including lesionectomy) and epilepsy/seizure diagnosis (ICD-9-CM 345.XX or 780.39). Children in the medically treated group had no prior surgical procedures for epilepsy and continued taking AEDs. For medically treated patients: refractory epilepsy patients were defined as those with refractory epilepsy treated with AEDs only. The screened AEDs were carbamazepine, divalproex, ethosuximide, ethotoin, felbamate, gabapentin, lacosamide, lamotrigine, levetiracetam, methsuximide, oxcarbazepine, perampanel, phenytoin, rufinamide, tiagabine, topiramate, valproic acid, vigabatrin, and zonisamide.[19]

Outcomes Measures

Primary outcomes evaluated were HU, the total number of AEDs, and death. HU was defined as the total postindex date healthcare utilization, including total IP visits, total ED visits, and total epilepsy- and seizure-related visits (include IP, ED, and ambulatory services visits). Total number of AEDs were defined as postindex AEDs, the total number of AEDs within postindex date 2 and 5 yr. Death was defined as death within 2 and 5 yr of the postindex date.

Other Variables

Patients' demographics were evaluated. Age was categorized into three groups: 0 to 4, 5 to 11, and 12 to 17 yr. Other demographics examined included gender (male and female), race (Non-Hispanic White, Non-Hispanic Black, Hispanic, and others), payer (Medicaid, private, and others), and sources of admission (hospital origin, clinic referral, other facility transferred, and unspecified).

Patients' clinical characteristics were evaluated, including the number of baseline AEDs, epilepsy diagnoses, and comorbidities. The number of AEDs before the index date was counted as the number of baseline AEDs. Epilepsy diagnoses were grouped into 3 categories: focal/partial epilepsy, generalized epilepsy, and unspecified. This was done to simplify the wide variety of epilepsy types into broad categories, allowing for comparison across epilepsy types and treatment groups, creating a larger sample size, allowing for wider generalizability, and inclusion of unspecified types which may or may not overlap with other types. Children with pediatric complex chronic conditions (P-CCCs) are reported to have higher health care utilization and more medical expenses than those without P-CCCs.[20] P-CCCs denote complex comorbid conditions in pediatric patients and include 12 categories: neurologic and neuromuscular, cardiovascular, respiratory, renal and urologic, gastrointestinal, hematologic or immunologic, metabolic, other congenital

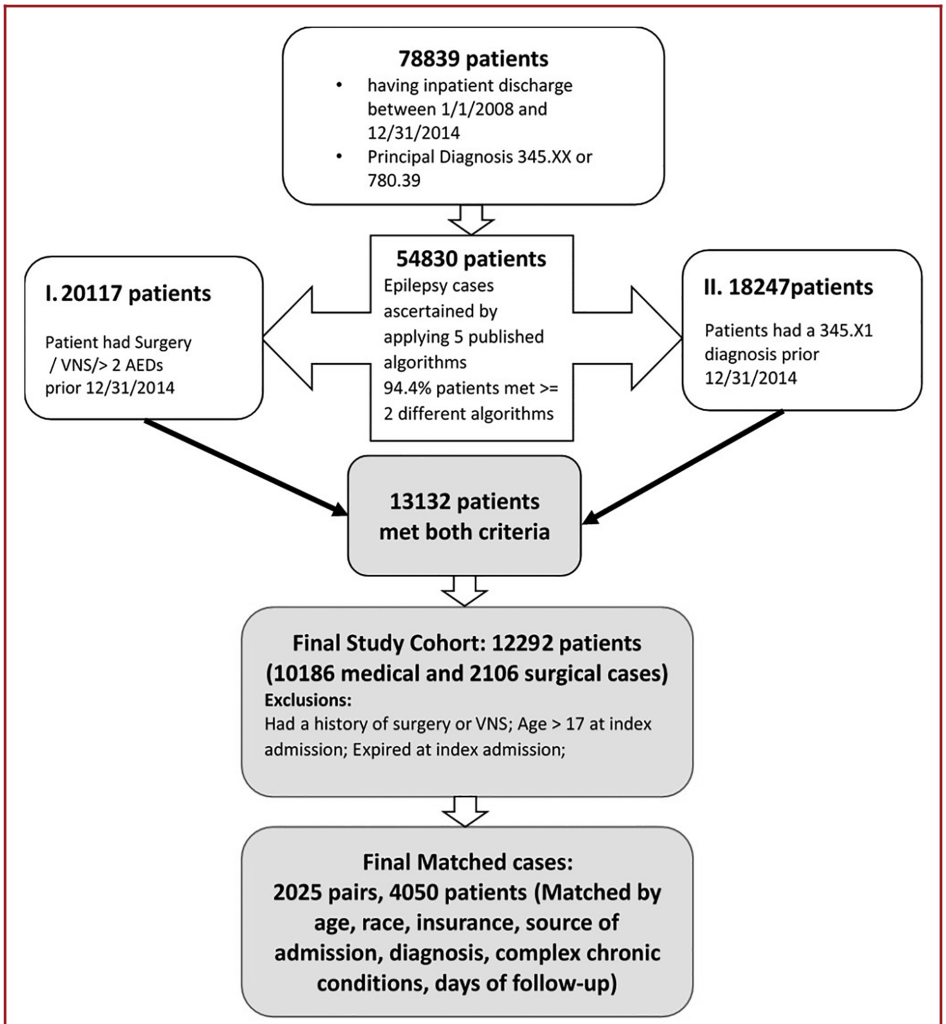

FIGURE 1. *Study consortium and flow diagram of patient selection which demonstrates patients identified at each step of defining the study cohort. The final study cohort comprised of 12292 patients, 10 186 medical, and 2106 surgical, of whom, 4050 were selected in 2025 matched pairs.*

or genetic defect, malignancy, premature and neonatal, technology dependent, and transplant. This study used the updated P-CCCs, version 2 in risk adjustment for matching surgically and medically treated patients.[21] Presence of P-CCCs was used as a binary variable in this study to classify patients by severity of comorbid conditions and overall health.

Additionally, the logistic regression model for calculating propensity scores (PS) included 2 "time" covariates: 1) follow-up time was the days between the date of index admission and the last visit at the hospital and 2) time from refractory epilepsy to index admission.

VNS was defined as the following: patients billed with an implanted stimulator (service codes 246135) or a current procedure code (64568) indicating a neurostimulator procedure along with epilepsy/seizure diagnosis (ICD-9-CM 345.XX or 780.39). As the mechanism of action of VNS remains unknown, and the ability to discern why patients were treated with VNS was unable to be elucidated through use of this administrative database, patients treated with VNS were not included in this study. Additionally, patients with incomplete data were excluded from this study.

Statistical Analysis

All subjects meeting inclusion criteria were then created into study groups, the size of which was based on those matched that met inclusion criteria. Comparisons between baseline groups for categorical data were made using chi square, or where indicated, Fisher's exact tests, and continuous data were compared using standard 2-sample *t*-test. Except we described mean of continuous variables for 2 groups, we also reported standardized differences (S-Diffs) to diagnose the balance of baseline characteristics between 2 samples as prior study suggested.[22] The PS matching method is used to create study groups that are similar to one another and remove bias due to observed covariates, which allowed for more precise assessment of the treatment effect in this observational

study.[23,24] The PS matching method[24] was used to control for potential confounding and bias for comparison of health outcomes of surgical patients to medically treated patients. Covariates associated with the probability of receiving surgical treatment were chosen in the logistic regression model for calculating PS. These covariates included age,[6] gender,[6] race,[6] insurance,[6] the source of admission, epilepsy diagnosis, and patients complex chronic conditions. Postindex follow-up time was added into the calculation of the PS as previous studies suggested[25-27] without diminution of the cohort size.[28] Surgically and medically treated patients were matched by PS with a caliper width of 0.1 times standard deviation (SD) of the PS logit using the greedy matching method.[29,30] Postmatched outcomes were assessed using a paired *t*-test if the differences of outcomes were normally distributed or the Wilcoxon Signed Rank test if the paired differences were non-normal. Statistical software SAS® 9.4 (SAS Institute Inc. 2013. Cary, North Carolina) and Stata 14.0 (StataCorp. 2015. *Stata Statistical Software: Release 14*. College Station, Texas) was used for data management and statistical analysis.

RESULTS

Baseline Covariates of Participants

A total of 12 292 children with refractory epilepsy meeting the criteria were identified. A total of 2106 (17.1%) and 10 186 (82.9%) were surgically and medically treated, respectively (Figure 1). Significant variations of subgroup distribution in age, race, insurance, source of admission, primary diagnosis and P-CCCs (for all binary tests, $P < .001$) were identified between medically and surgically treated patients. Patients receiving surgical treatment were older (mean age = 8.9-yr old, SD = 5.2), were predominantly non-Hispanic White (69.8%), with private insurance (52.0%), coming from hospital origin and clinic referral (80.9%), with local/partial epilepsy (54.4%), and having P-CCCs (97.8%) compared to medically treated patients (mean age 7.4-yr old, SD 5.0; 60.4% non-Hispanic White, 40.2% private insurance, 71.2% hospital origin and clinic referral, 25.4% focal/partial epilepsy, and 87% having P-CCCs) (Table 1).

Descriptive Data After PS Matching

Before PS matching, the standard differences were high in the follow-up period, insurance, primary diagnosis, and complex chronic conditions between medically and surgically treated groups. The S-Diff of logit PS scores is 0.97918. After PS-matched, 4050 cases were included, 2025 per each treated group; the percent of S-Diff of logit PS reduction was 99.94%. The matched S-Diff of matched variables showed that the medically and surgically treated group are well-matched (Table 2). The variations of subgroup distributions were insignificant between the two groups. 58% vs 57% and 22% vs 25% of medical vs surgical patients were followed up at 2 and 5 yr.

Outcomes Comparisons

A total of 47 (2.3%) and 9 (0.44%) cases in medically and surgically treated groups died within the follow-up period, respectively. Overall survival rates were 98.07% and 99.58% at 2 yr and 96.66% and 98.99% at 5 yr for medically and surgically treated patients, respectively.

Within 2 yr of the postindex date, the number of IP visits was 1.9 and 1.2, of ED visits were 1.4 and 0.7 for medically and surgically treated patients, respectively. The number of epilepsy associated visits (IP, ED, and ambulatory visits) was 1.9 and 1.1. Within 5 yr of the postindex date, the number of IP visits was 3.9 and 2.5, ED visits 3.2 and 1.7, for medically and surgically treated patients, respectively. The number of epilepsy associated visits (IP, ED, and ambulatory visits) was 6.4 and 3.9 (Table 3).

The number of AEDs used at the index date (baseline) were indifferent between medically (mean = 3.24, STD = 1.15, median = 3, IQR = 1) and surgically (mean = 3.22, STD = 1.48, median = 3, IQR = 1) treated patients. The number of AEDs in the first year for the surgically treated group significantly dropped compared to medically treated patients. (Surgical cases: 3.22 decreased to 2.59; Medical cases: 3.24 decreased to 3.06). At the 2-yr postindex date, 608 of 1188 (51.4%) medical and 426 of 1168 (36.7%) surgical patients had recorded AED use, the average number of AEDs were 2.82 and 2.37 for medically and surgically treated patients, respectively. At the 5 yr of the postindex date, 149 of 461 (31.9%) and 121 of 520 (23.3%) patients had recorded AED use, the average number of AEDs were 2.92 and 2.46, respectively (Table 3).

The cumulative number of visits from year 1 to year 5 are shown in Figure 2. Medically treated patients have significantly higher postindex health utilization than surgically treated patients in seizure, epilepsy associated visits and all types of hospital visits.

DISCUSSION

To our knowledge, this study is the first of its kind to evaluate, not only clinical outcomes comparing surgically to medically managed pediatric epilepsy, but to examine related healthcare utilization.

Key Findings

There are several unique findings from this analysis. Table 1 shows baseline clinical characteristics of surgically and medically treated groups; there are significant differences in demographic and clinical characteristics. Several of these patients' characteristics suggest the impact of payor and race on access to medical care in the US. There are described health disparities across race, insurance, and ethnicity in the US especially with respect to pediatric subspecialty surgical care.[31-37] The specific reasons contributing to such disproportions in subgroups are not known in this study design and dataset. Additionally, the presence of P-CCCs and origin of referral from a hospital or clinic suggest that those already requiring medical attention have lower barriers of access to surgical subspecialty evaluation and treatment.

One of the main outcomes examined was survival. Surgically and medically treated pediatric epilepsy patients had comparable survival rates at 2-yr follow-up. By 5 yr follow up, the survival rate is significantly different among the groups, with surgically treated

TABLE 1. Baseline Patient Characteristics

Variables	n	Medical (n = 10 186)		Surgical (n = 2106)		*P* value
Follow-up period (d)	12 292	M = 1390	SD = 1005	M = 1086	SD = 1012	<.001
Time from identified date of refractory epilepsy to index date	12 292	M = 537	SD = 719	M = 388	SD = 535	<.001
Number of AEDs prior 1 yr of index date	12 172	M = 3.3	SD = 1.2	M = 3.2	SD = 1.5	<.001
Age in yr	12 292	M = 7.4	SD = 5.0	M = 8.9	SD = 5.2	<.001
		N	%	N	%	
Age in yr						<.001
0-4	4104	3570	35.1	534	25.4	
5-11	4952	4134	40.6	818	38.8	
12-17	3236	2482	24.4	754	35.8	
Gender						.430
Male	6587	5442	53.4	1145	54.4	
Female	5705	4744	46.6	961	45.6	
Race and ethnicity						<.001
Non-Hispanic White	7622	6153	60.4	1469	69.8	
Non-Hispanic Black	1565	1378	13.5	187	8.9	
Hispanic	2102	1813	17.8	289	13.7	
Others	1003	842	8.3	161	7.6	
Insurance						<.001
Medicaid	5658	4931	48.4	727	34.5	
Private	5193	4099	40.2	1094	52.0	
Others	1441	1156	11.4	285	13.5	
Sources of admission						<.001
Hospital	6949	5721	56.2	1228	58.3	
Clinic referral	2003	1528	15.0	475	22.6	
Other transferred	1634	1422	14.0	212	10.1	
Unspecified	1706	1515	14.9	191	0.1	
Primary diagnosis						<.001
Focal/partial	3731	2586	25.4	1145	54.4	
Generalized	1850	1722	16.9	128	6.1	
Unspecified	6711	5878	57.7	833	39.6	
Complex chronic conditions						<.001
No	1373	1327	13.0	46	2.2	
Yes	10 919	8859	87.0	2060	97.8	

Abbreviation: AED = antiepileptic medications; N = number of cases; M = mean; SD = standard deviation.

pediatric epilepsy patients having higher survival ($P < .0001$). Epilepsy not only impacts quality of life and clinical health: there are quantifiable consequences on mortality. Typically, the risk of sudden unexplained death in epilepsy (SUDEP) continues at up to 1% per year in those who do not have adequate seizure control.[38,39]

An important finding in this study is the impact surgically treated epilepsy has on HU compared to medically treated epilepsy. Over time, the number of IP, ED, ambulatory, and epilepsy or seizure associated visits decreased in the surgically treated group. We also found that the number of AEDs patients were on decreased over time in both groups, but significantly decreased in the first year in the surgical group compared to the medical group. Overall, with decreased hospital visits and medications, the surgically treated group was found to have decreased HU over time compared to the medically treated group.

Interpretation

Our study identified an improved survival, reduced AED use, and reduced HU over time in those treated surgically. Therefore, we underscore the importance of referral to a surgical epilepsy center for all pediatric patients with refractory epilepsy. There is a heightened urgency to achieve seizure freedom in children when compared with adults as there is a significant association between childhood seizures and developmental arrest/regression, particularly in children less than 2 yr of age.[40] Early surgical intervention has been shown that to limit the time on intolerable medications, avoid cognitive delays and learning disabilities, and minimize the lifelong effects of uncontrolled epilepsy.[40]

TABLE 2. Patient Characteristics and S-Diffs of Baseline Covariates

	Medical (n = 2025)		Surgical (n = 2025)			S-Diffs	
Matched model	**n**	**%**	**n**	**%**	***P* value**	**Matched**	**Unmatched**
Follow-up period (d)	M = 1107	SD = 929	M = 1113	SD = 1014	.838	0.006	0.300
Time from identified date of refractory epilepsy to index date	M = 386	SD = 612	M = 397	SD = 540	.674	0.012	0.223
Number of AEDs prior 1 yr of index date	M = 3.2	SD = 1.2	M = 3.2	SD = 1.5	.687	0.012	0.071
Age in yr					.969		
0-4	520	25.7	527	26.0		0.008	0.217
5-11	804	39.7	800	39.5		0.004	0.036
12-17	701	34.6	698	34.5		0.003	0.256
Gender					1.000		
Male	1094	54.0	1094	54.0		0.000	0.189
Female	931	46.0	931	46.0		0.000	0.189
Race and ethnicity					.926		
Non-Hispanic White	1392	68.7	1395	68.9		0.003	0.196
Non-Hispanic Black	197	9.7	186	9.2		0.017	0.146
Hispanic	275	13.6	284	14.0		0.012	0.111
Others	161	8.0	160	7.9		0.001	0.023
Insurance					.717		
Medicaid	711	35.1	718	35.5		0.007	0.285
Private	1022	50.5	1033	51.0		0.011	0.236
Others	292	14.4	274	13.5		0.026	0.068
Sources of admission					.517		
Hospital	1159	57.2	1185	58.5		0.026	0.038
Clinic referral	469	23.2	440	21.7		0.037	0.200
Other transferred	193	9.5	209	10.3		0.024	0.123
Unspecified	204	10.1	191	9.4		0.021	0.176
Primary diagnosis					.946		
Local/partial	1075	53.1	1075	53.1		0.000	0.621
Generalized	133	6.6	128	6.3		0.008	0.342
Unspecified	817	40.4	822	40.6		0.005	0.371
Complex chronic conditions					.476		
No	53	2.6	46	2.3		0.013	0.415
Yes	1972	97.4	1979	97.7		0.013	0.415

AED = Antiepileptic Medications; N = number of cases; M = mean; SD = standard deviation.

Unfortunately, there is a well-documented delay in referral to epilepsy centers for surgical evaluation, with possibly less than 1% of patients with refractory epilepsy being referred to epilepsy centers.[41] There are many considerations as to why more patients with refractory epilepsy may not be referred to epilepsy centers. Cost considerations, management being outsourced to the community, and misconceptions in regards to who may benefit from surgery, are among the most common reasons for lack of or delayed referrals.[41] Survey of caregivers of children with refractory epilepsy demonstrated that those who waited a shorter period of time (1 yr) for surgery were more satisfied, than those who waited almost 4 yr: the latter group wished their child's surgery had occurred sooner.[42] Improved healthcare utilization, neurocognitive and clinical outcomes for the reasons described above and the potential increased risk of SUDEP year over year, accentuates the need for increased and early referrals to specialized epilepsy centers, and a reduction in time to surgery for those that may benefit.

There are directions for the future for primary care and subspecialty providers: from an overall child health standpoint, improving referral patterns for specialized and surgical evaluation is imperative to limit the deleterious effects of ongoing seizures in the developing brain, so as to decrease the time to surgery from seizure onset. With all of the continued innovation in the field of pediatric epilepsy surgery, it is important that continued strides be made in patient recruitment and early referral to enhance clinical outcomes and quality of life in the future.

TABLE 3. Healthcare Utilization

Variable (n = 2025 pairs)	Treatment	Calculation base - Number of cases left at year 2 and year 5: Number of cases left	Mean (SD)	Median	IQR	*P* value	Calculation base - Entire cohort: Mean (SD)	Median	IQR	*P* value
3A: Post index IP, ED, and ambulatory services										
Post IP visits within 2 yr	Medical	1188	1.9(2.8)	1	3	<.001	1.5(2.4)	1	2	<.001
	Surgical	1168	1.2(1.8)	0	2		0.9(1.5)	0	1	
Post ED visits within 2 yr	Medical	1188	1.4(2.5)	0	2	<.001	1.0(2.2)	0	1	<.001
	Surgical	1168	0.7(1.5)	0	1		0.5(1.3)	0	1	
Post Epilepsy associated IP visits within 2 yr	Medical	1188	1.9(2.7)	1	2	<.001	1.5(2.3)	1	2	<.001
	Surgical	1168	1.1(1.7)	0	2		0.8(1.4)	0	1	
Post Epilepsy associated ED visits within 2 yr	Medical	1188	0.8(1.7)	0	1	<.001	0.4(1.1)	0	0	<.001
	Surgical	1168	0.4(1.1)	0	0		0.2(0.6)	0	0	
Post Epilepsy associated visits within 2 yr	Medical	1188	3.0(3.7)	2	3	<.001	2.4(3.4)	1	3	<.001
	Surgical	1168	1.7(2.4)	1	2		1.3(2.1)	0	2	
Post IP visits within 5 yr	Medical	461	3.9(4.7)	3	4	<.001	2.4(3.8)	1	3	<.001
	Surgical	520	2.5(2.9)	2	4		1.5(2.4)	1	2	
Post ED visits within 5 yr	Medical	461	3.2(5.3)	1	4	<.001	1.8(3.7)	0	2	<.001
	Surgical	520	1.7(2.9)	1	2		0.9(2.3)	0	1	
Post epilepsy associated IP visits within 5 yr	Medical	461	3.8(4.7)	2	4	<.001	2.3(3.6)	1	3	<.001
	Surgical	520	2.4(2.8)	2	3		1.4(2.2)	0	2	
Post epilepsy associated ED visits within 5 yr	Medical	461	1.7(3.1)	1	2	<.001	0.7(1.8)	0	1	<.001
	Surgical	520	0.9(1.9)	0	1		0.4(1.1)	0	0	
Post epilepsy associated visits within 5 yr	Medical	461	6.4(6.8)	4	7	<.001	3.8(5.3)	2	3	<.001
	Surgical	520	3.9(4.2)	3	4		2.2(3.4)	1	3	

Time points of estimates	Treatment	Calculated base	Number of cases left	% with AEDs recorded[a]	Mean	SD	MIN, MAX	Median	IQR	*P* value
3B: Antiepileptic drugs comparison										
Baseline	Medical	2025	2025	100.00	3.240	1.150	1, 8	3	1	.687
	Surgical	2025	2025	100.00	3.223	1.479	1, 11	3	2	
Post 1 yr	Medical	1052	1413	74.45	3.059	1.376	1, 9	3	2	<.001
	Surgical	719	1317	54.76	2.591	1.369	1, 9	2	1	
Post 2 yr	Medical	608	1188	51.35	2.817	1.298	1, 9	3	2	<.001
	Surgical	426	1168	36.69	2.369	1.326	1, 8	2	2	
Post 3 yr	Medical	383	969	39.57	2.885	1.285	1, 8	3	2	<.001
	Surgical	253	955	26.69	2.387	1.318	1, 7	2	2	
Post 4 yr	Medical	229	700	32.53	2.882	1.324	1, 8	3	2	<.001
	Surgical	179	737	24.39	2.341	1.316	1, 8	2	2	
Post 5 yr	Medical	149	461	31.91	2.919	1.402	1, 7	3	2	.004
	Surgical	121	520	23.31	2.463	1.088	1, 6	2	1	

[a]% of AEDs records = calculated base/number of cases left ∗100.

Abbreviations: AEDs = antiepileptic medications; SD = standard deviation; MIN = minimum; MAX = maximum; IQR = interquartile range; N: number of cases; ED = emergency department.

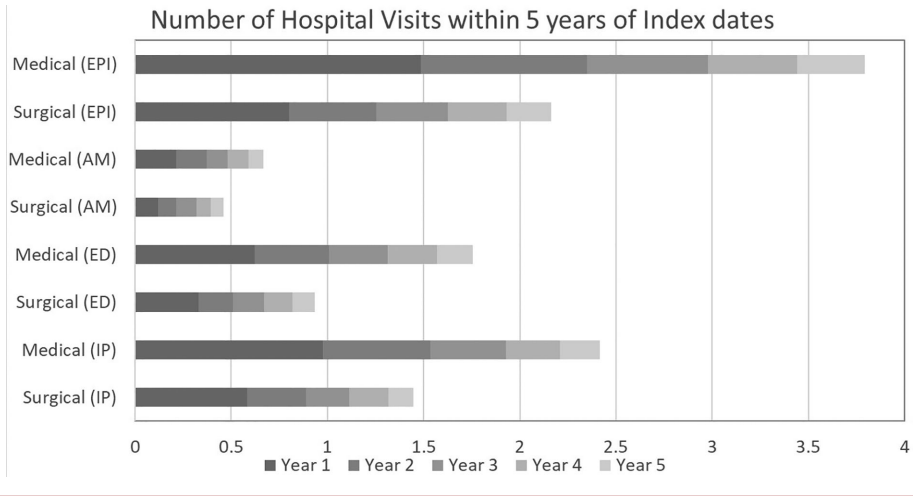

FIGURE 2. *Number of hospital visits, for epilepsy related, ambulatory, ED, and IP visits, trended over 5 yr postindex, demonstrate reduction in visits in the surgical group compared to the medical group.*

Limitations

There are several limitations to this study. Inherent in the use of administrative data, there may be errors in coding or documentation at the time of each visit. This is mitigated by the internal data verification process to uphold the quality of the well-regarded PHIS program, as well as the reality of economic transactions: billable services, products, and drugs are likely to be recorded. The granularity of clinical detail and rationale for clinical decision-making cannot be gleaned from these data. Codes in existence for the epoch under study do not define specifications for techniques such as stereoelectroencephalography with depth electrodes or magnetic resonance imaging-guided laser interstitial thermal therapy, so these techniques cannot be studied separately. Additionally, while our analysis can establish correlations, causal relationships cannot be explained due to the limitation of observational data.

From an epilepsy treatment standpoint, use of administrative data cannot substitute for a clinical research study. However, such a nationwide view can, in turn, provide patterns for further examination in clinical practice settings and may inform future clinical trial design when appropriate. While there are established published methods for defining a cohort with refractory epilepsy from administrative data, we acknowledge the study design to set up comparison groups required dates of initial diagnosis and dates for washout periods and for follow-up. In reality, such dates of initial diagnosis for refractory epilepsy are less well-defined in medical records as medication-resistant epilepsy is a chronic illness. As such, this disease carries a high toll on patients and their families' health and quality of life, and continued research from basic science, translational, clinical trial, health services, and policy perspectives are warranted.

Generalizability

As we controlled for confounding variables through matching, we believe that the findings in our study hold internal validity. Furthermore, we believe that our findings are readily generalizeable to similar groups of children given the broad patient population examined in this study, across the United States, from various ethnic, racial, and socioeconomic backgrounds, that are representative of the larger target population of pediatric patients with refractory epilepsy.

CONCLUSION

We present an analysis of the Children's Hospital Association PHIS database examining the outcomes of surgically and medically treated refractory epilepsy in the pediatric population. We explore outcomes related to clinical outcomes, survival, antiepileptic use, and healthcare utilization. We demonstrate a decrease in ED visits, IP admissions, epilepsy associated visits, and AED use over short-term and long-term follow up in the surgical group compared to the medical group. This suggests a long-term decrease in HU in the group that received epilepsy surgery. Favorable clinical outcomes and substantial implications for both short- and long-term effectiveness emphasizes the importance of the role of epilepsy surgery in the treatment of refractory epilepsy in children.

Disclosures

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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COMMENT

In this retrospective study, patients with refractory epilepsy treated with surgery had significant reductions in healthcare utilization compared with matched patients treated with antiepileptic medications only. The cost effectiveness was noticed in terms of medication use, inpatient admissions and outpatient resource utilization- such as clinic, ambulatory, and emergency visits. This study demonstrates that surgical treatment of epilepsy provides long-term improved control of epilepsy as well as reduced healthcare utilization, hospital visits, medication use, and ambulatory/emergency visits among pediatric patients with refractory epilepsy compared to those treated medically.

The authors must be commended for this excellent contribution to our field, highlighting, from a public health and individual aspects, the cost effectiveness of early interventions in medically refractory epilepsy. The work sets the tone for future studies addressing similar questions. Medically refractory epilepsy represents a tremendous burden for millions of individuals and families. Surgery should not be postponed when rightfully indicated. Early intervention will provide better chances for seizure control and greatly mitigate the economic burden of this devastating disease. Congratulations to the authors for the contribution.

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