Time to pediatric epilepsy surgery is related to disease severity and nonclinical factors

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ABSTRACT

Objective: To identify clinical and nonclinical factors associated with time from epilepsy onset to surgical evaluation and treatment among a cohort of children having epilepsy surgery.

Methods: Data were abstracted from records of 430 children (younger than 18 years) who had epilepsy neurosurgery at the University of California, Los Angeles from 1986 to 2010. Multivariable Cox proportional hazards models were used to analyze unique associations of clinical severity, pre-referral brain MRI, and sociodemographic characteristics with time to surgery.

Results: Shorter time to surgery was associated with active (hazard ratio [HR] 5.67, 95% confidence interval [CI] 3.74–8.70) and successfully treated infantile spasms (HR 2.20, 95% CI 1.63–2.96); daily or more seizures (HR 2.09, 95% CI 1.58–2.76); MRI before referral regardless of imaging findings (HR 1.95, 95% CI 1.47–2.58); private insurance (HR 1.54, 95% CI 1.14–2.09); and Hispanic ethnicity (HR 1.38, 95% CI 1.01–1.87). There were race/ethnicity by insurance interactions (log-rank $p = 0.049$) with shortest time to surgery for Hispanic children with private insurance.

Conclusions: Shorter intervals to surgical treatment were associated with greater epilepsy severity and insurance type, consistent with existing literature. However, associations of shorter times to treatment with having a brain MRI before referral and Hispanic ethnicity were unexpected and warrant further investigation. More knowledgeable referring providers and parents with greater help-seeking capability may explain obtaining an MRI before referral. Shorter intervals to surgery among Hispanic children may relate to the same factors yielding an increased volume of Hispanic children receiving surgery at the University of California, Los Angeles since 2000. *Neurology*® **2013;80:1231–1239**

GLOSSARY

AED = antiepileptic drug; **CCS** = California Children's Services; **CI** = confidence interval; **HIPAA** = Health Insurance Portability and Accountability Act; **HR** = hazard ratio; **IS** = infantile spasm; **LA** = Los Angeles; **UCLA** = University of California, Los Angeles.

Epilepsy surgery is recognized as a safe and effective treatment option for children with medically intractable epilepsies associated with structural lesions.[1–8] Timely referral may be important because preliminary evidence suggests that shorter intervals from epilepsy onset to surgery are associated with better short-term cognitive outcomes.[9,10] However, a substantial proportion of children do not receive surgery in a timely manner.[11,12] Furthermore, during testimony for the Institute of Medicine report on epilepsy, parents of children with epilepsy reported concern regarding delays in receipt of epilepsy specialty care, including surgery.[13]

We previously found that children with infantile spasms (IS) had shorter intervals from seizure onset to surgery compared with those without spasms.[9] However, the impact of other clinical and nonclinical factors with time to surgery for pediatric patients has not been explored. Although studies have demonstrated sociodemographic disparities in the utilization of temporal lobectomy, none have examined whether such factors mediate delays in time to surgery in children.[14–17] To elucidate factors associated with timing of referral and surgery among children with epilepsy, we utilized a large cohort from the University of California, Los Angeles (UCLA) who had surgery over the past 25 years. Based on prior literature in children and adults, we hypothesized that

increased epilepsy severity as documented by a history of IS and a greater seizure frequency, abnormal pre-referral brain MRI, private insurance, and non-Hispanic, white race/ethnicity would be associated with shorter time to surgery.

METHODS Sample. This sample was drawn from a consecutive series of 605 children (younger than 18 years at surgery) who had epilepsy surgery at UCLA (January 1986 to December 2010). Excluded were children who had palliative procedures (vagus nerve stimulation and corpus callosotomy; n = 143), craniotomy without resection (biopsy only; n = 4), diagnostic intracranial electrodes without resection (n = 4), and multiple subpial transections without cortical resection (n = 1); patients who were "self-pay" (uninsured but with financial means to pay, primarily of international residence; n = 23) were also excluded. The final cohort for our analytic sample was 430 children. If a child had multiple procedures, data regarding only the first resection were analyzed. Children who underwent presurgical evaluation but were not deemed candidates for resective surgery and those who were offered surgery but whose parents declined the procedure were not captured in this surgical database.

Standard protocol approvals, registrations, and patient consents. The UCLA Institutional Review Board approved this study. Patients or families signed research informed consents and Health Insurance Portability and Accountability Act (HIPAA) authorizations. Before HIPAA enactment, this study was considered exempt from requiring research informed consent. This study is not a clinical trial.

Data collection. Clinical, sociodemographic, and pre-referral diagnostic data were obtained by abstraction of outpatient and inpatient medical records, EEG including video-EEG telemetry reports, UCLA and non-UCLA radiology studies, operative/scheduling reports, histopathology reports, and UCLA encounter/registration forms. Encounter and registration forms include home address, insurance, race/ethnicity, and preferred language, obtained by an administrative assistant before a visit.

Clinical and diagnostic variables. Details regarding the standardized presurgical evaluation protocols, surgical procedures, and clinical variables have been previously described.[3,9,12] Clinical variables included date of epilepsy onset and surgery; seizure frequency before surgery (daily seizures or more vs less than daily); type of surgery (hemispherectomy, multilobar, and lobar/focal resection); presurgical history of IS as determined by clinical history and EEG criteria of hypsarrhythmia or modified hypsarrhythmia (history of active spasms at surgery, successfully treated spasms, or no history of spasms); number of antiepileptic drugs (AEDs) at the time of presurgical evaluation (0–1, 2, or ≥3); side of surgery; and etiology (determined by UCLA neuroimaging and histopathology). Etiology was defined as neurodevelopmental (cortical dysplasia, hemimegalencephaly, and tuberous sclerosis complex) or non-neurodevelopmental (cortical atrophy, hippocampal sclerosis, infection, Rasmussen encephalitis, tumor, and nondiagnostic). We abstracted whether a child had a pre-referral brain MRI (yes vs no/unknown), and whether the prior imaging was normal or abnormal related to epilepsy etiology/surgical target.

"Time to surgery" was calculated as the interval from date of epilepsy onset to date of epilepsy surgery, and "time to referral" was the interval from date of epilepsy onset to the date of the first appointment at UCLA for evaluation for refractory epilepsy (with a neurologist or neurosurgeon). Because UCLA is a tertiary care center, nearly all children in this cohort had treatment initiated before referral to UCLA.

Sociodemographic variables. Insurance type at the time of referral, race/ethnicity, sex, primary residence, and preferred language were abstracted from UCLA records. Insurance was categorized as Preferred Provider Organization, Health Maintenance Organization, indemnity, Medicaid (MediCal in California), and California Children's Services (CCS). Insurance type was dichotomized into private (Preferred Provider Organization, Health Maintenance Organization, indemnity) or government insurance (Medicaid/CCS). There were no uninsured children in this cohort (UCLA does not offer pro bono care). Race/ethnicity was classified as non-Hispanic white, Hispanic, or other (African American, Asian, or Middle Eastern). Geographic residence was classified using zip codes (Los Angeles [LA] County or not).

Analysis. Bivariate comparisons were made using appropriate statistical tests (χ^2, Pearson correlations for dichotomous and ordered variables, analysis of variance, and log-rank test with Kaplan-Meier survival analysis). Multivariable survival analysis using Cox proportional hazards models was used to examine the relative association of clinical, diagnostic, and sociodemographic variables with dependent variables (time to surgery, time to referral, and time from referral to surgery) in separate regression models, controlling for date of surgery, grouped into 5-year intervals. Dummy variables were created for categorical nondichotomous independent variables (history of IS, number of AEDs, race/ethnicity). Dichotomous and ordered covariates had correlations of $r \leq |0.50|$ with each other. The relative associations of the following clinical, pre-referral diagnostic, and sociodemographic variables with dependent variables were examined: history of active IS or treated IS (reference: no history of IS), daily seizures or more (reference: less than daily seizures), neurodevelopmental etiology (reference: non-neurodevelopmental etiology), 0 to 2 AEDs (reference: ≥3 AEDs), age at epilepsy onset, pre-referral MRI (reference: no/unknown MRI), male (reference: female), Hispanic or other ethnicity (reference: non-Hispanic white), and private insurance (reference: Medicaid/CCS).

To assess potential mediating effects of associations (hazard ratios [HRs]) of race/ethnicity with time to surgery and to referral, LA County residence and language were each separately added as a covariate to the models described previously. The magnitude of these HRs was compared with those models without that corresponding variable. The relationships of ethnicity and insurance with time to surgery and time to referral were further examined using a log-rank test to assess significance of time to surgery and of time to referral across 4 race-insurance categories (Hispanic-private, Hispanic-government, non-Hispanic white–private, and non-Hispanic white–government; n = 389); between-category differences were tested using a separate Cox proportional hazards test.

To elucidate whether having a pre-referral MRI vs having an abnormal finding on a pre-referral MRI was associated with dependent variables, we reanalyzed the main models replacing whether or not the child had a pre-referral MRI with dummy variable indicators for whether the MRI was normal or abnormal regarding epilepsy etiology/surgical target (reference: no/unknown pre-referral MRI). Because all children in this cohort by definition had surgery before age 18 years, we conducted a sensitivity analysis to determine whether any observed association of age at onset to time to surgery or to referral was a function of study design; models were reanalyzed excluding children aged 10 years or older at epilepsy onset.

All analyses were performed using Stata software (11.0; StataCorp, College Station, TX), setting an a priori p value ≤0.05 for significance.

RESULTS Clinical, diagnostic, and sociodemographic characteristics of this cohort are shown in table 1

Table 1	Characteristics of children who had epilepsy surgery (N = 430)[a]
	n (%) or mean (SD); median (IQR)
Dependent variables	
Time from epilepsy onset to surgery, y	4.45 (3.86); 3.25 (1.33–6.66)
Time from epilepsy onset to referral, y	3.30 (3.49); 2.00 (0.62–4.92)
Time from referral to surgery, y	1.15 (1.85); 0.44 (0.20–1.21)
Year of surgery, within 5-y intervals	
1986–1990	59 (13.7)
1991–1995	87 (20.2)
1996–2000	54 (12.6)
2001–2005	106 (24.7)
2006–2010	124 (28.8)
Clinical	
History of infantile spasms	
Active infantile spasms (at time of surgery)	45 (10.5)
Successfully treated infantile spasms (focal epilepsy)	99 (23.0)
No history of infantile spasms	286 (66.5)
Seizure frequency, daily or more	337 (79.4)
Side of surgery, left	221 (51.4)
Epilepsy operation type	
Hemispherectomy	176 (41.6)
Lobar/focal	184 (43.5)
Multilobar	64 (15.1)
Etiology, ND (CD, HME, TSC)[b]	208 (51.5)
No. of AEDs at time of surgery	
0–1	71 (17.2)
2	156 (37.9)
≥3	185 (44.9)
Age at epilepsy onset, y	2.48 (3.32); 0.75 (0.25–4.0)
Diagnostic	
Completed brain MRI before referral[c]	327 (76.0)
Sociodemographic	
Male	228 (53.0)
Race/ethnicity	
Non-Hispanic white	317 (76.9)
Hispanic	82 (19.2)
Other[d]	29 (6.8)
Private insurance (PPO, HMO, indemnity)[e]	329 (78.3)
Los Angeles County resident	109 (25.4)
English-language preference of parent	397 (92.3)

Abbreviations: AEDs = antiepileptic drugs; CD = cortical dysplasia; HME = hemimegalencephaly; HMO = Health Maintenance Organization; IQR = interquartile range; ND = neurodevelopmental; PPO = Preferred Provider Organization; TSC = tuberous sclerosis complex.
[a] Missing data for seizure frequency (n = 6), operation type (n = 7), etiology (n = 26), number of AEDs (n = 18), race/ethnicity (n = 2), and insurance type (n = 10). Less than daily seizure frequency includes weekly (n = 72) and less than weekly (n = 16).
[b] ND etiology includes HME (n = 31), CD (n = 151), and TSC (n = 26); other non-ND etiologies include atrophy (n = 55), hippocampal sclerosis (n = 33), infection (n = 17), Rasmussen encephalitis (n = 33), tumor (n = 38), and nondiagnostic (n = 22).
[c] No (or unknown if completed) brain MRI before referral = 103.
[d] Other race includes African American (n = 6), Middle Eastern (n = 3), and Asian (n = 20).
[e] Private insurance includes PPO (n = 171), HMO (n = 81), and indemnity (n = 77); non-private (government) includes Medicaid (n = 91).

and in table e-1 on the *Neurology*® Web site at www.neurology.org. Children with IS (active and successfully treated in 1 group) had median times to referral (0.88 vs 2.99 years) and to surgery (1.41 vs 4.42 years) that were shorter compared with those without a history of IS.

In multivariate analysis, shorter time from epilepsy onset to surgery was associated with active (HR 5.67, 95% confidence interval [CI] 3.74–8.60) and successfully treated IS (HR 2.20, 95% CI 1.63–2.96) (vs no history of IS); daily or more seizure frequency (HR 2.09, 95% CI 1.58–2.76) (vs less than daily seizure); MRI before referral (HR 1.95, 95% CI 1.47–2.58) (vs no/unknown MRI); private insurance (HR 1.54, 95% CI 1.14–2.09) (vs Medicaid); Hispanic ethnicity (HR 1.38, 95% CI 1.01–1.87) (vs non-Hispanic white); and older age of epilepsy onset (HR 1.09, 95% CI 1.05–1.14; table 2).

A similar pattern was seen for factors associated with time to referral except for 3 differences (table 2). Longer time to referral was associated with operations from 2006 to 2010 (vs 1986–1990) (HR 0.55, 95% CI 0.37–0.83; $p = 0.004$) and taking 2 AEDs (vs 0 or 1 AED) (HR 0.66, 95% CI 0.48–0.90; $p = 0.009$). In addition, the association of Hispanic ethnicity with shorter time to referral was of a smaller magnitude and not significant (HR 1.27, 95% CI 0.94–1.73; $p = 0.12$). Shorter times from referral to surgery were associated with active IS (vs no history of IS) and having a pre-referral MRI (table 2).

Because Hispanic children were more likely to live in LA County (χ^2; $p < 0.001$) and have parents whose preferred language was not English (χ^2; $p < 0.001$), we examined whether geographic residence and language might be mediators of the associations we observed between Hispanic race/ethnicity and shorter time to surgery. There was a slight lessening of the association between Hispanic ethnicity and time to surgery in the model comparing LA with non-LA County residence (HR 1.33 vs 1.38; table e-2). Adding preferred language resulted in higher magnitudes of HRs for the associations of Hispanic ethnicity with shorter time to surgery (HR 1.46 vs 1.38) and to referral (HR 1.31 vs 1.27). Children living in LA County had longer times from referral to surgery (table e-2).

The relationships of ethnicity and insurance were further examined across 4 race-insurance categories (Hispanic-private, Hispanic-government, non-Hispanic white–private, and non-Hispanic white–government; n = 389). There were ethnicity-insurance group differences in time to surgery (log-rank test $p = 0.049$) and to referral (log-rank test $p = 0.097$; table 3). Regarding specific between-group differences, shorter times were associated with Hispanic ethnicity and private insurance compared with non-Hispanic

Table 2 Associations of time to surgery, time to referral, and time from referral to surgery with clinical, diagnostic, and demographic variables[a]

	Time to surgery		Time to referral		Time from referral to surgery	
	HR (95% CI)	p	HR (95% CI)	p	HR (95% CI)	p
Clinical variables						
Infantile spasms (ref.: no spasms)						
Active spasms	5.67 (3.74–8.60)	<0.001[b]	5.45 (0.38–8.31)	<0.001[b]	1.77 (1.19–2.64)	0.005[b]
Successfully treated spasms	2.20 (1.63–2.96)	<0.001[b]	2.25 (1.67–3.05)	<0.001[b]	1.18 (0.87–1.59)	0.29
Daily or more seizures (ref.: <daily)	2.09 (1.58–2.76)	<0.001[b]	2.14 (1.61–2.85)	<0.001[b]	1.09 (0.82–1.44)	0.55
Etiology ND (ref.: non-ND)	1.22 (0.95–1.56)	0.11	1.22 (0.96–1.55)	0.11	1.15 (0.88–1.50)	0.31
No. of AEDs at surgery (ref.: 0–1)						
2 AEDs	0.80 (0.59–1.09)	0.17	0.66 (0.48–0.90)	0.009[b]	1.11 (0.81–1.53)	0.50
≥3 AEDs	0.98 (0.72–1.34)	0.90	0.88 (0.64–1.22)	0.45	1.11 (0.81–1.52)	0.50
Age of epilepsy onset	1.09 (1.05–1.14)	<0.001[b]	1.09 (1.05–1.14)	<0.001[b]	0.99 (0.95–1.03)	0.65
Diagnostic variables						
MRI before referral (ref.: no/unknown)	1.95 (1.47–2.58)	<0.001[b]	1.79 (1.34–2.38)	<0.001[b]	1.41 (1.06–1.89)	0.02[b]
Demographic variables						
Male	1.20 (0.97–1.49)	0.09	1.09 (0.87–1.35)	0.45	1.13 (0.90–1.42)	0.28
Race (ref.: non-Hispanic white)						
Hispanic	1.38 (1.01–1.87)	0.04[b]	1.27 (0.94–1.73)	0.12	1.13 (0.82–1.54)	0.46
Other	0.77 (0.51–1.16)	0.21	0.88 (0.59–1.33)	0.55	0.93 (0.62–1.40)	0.73
Private insurance (ref.: Medicaid)	1.54 (1.14–2.09)	0.005[b]	1.47 (1.09–1.99)	0.01[b]	1.20 (0.89–1.63)	0.22
Year of surgery cohort (ref.: 1986–1990)						
1991–1995	0.86 (0.57–1.31)	0.49	0.69 (0.46–1.04)	0.08	1.15 (0.75–1.77)	0.51
1996–2000	1.18 (0.75–1.86)	0.47	1.13 (0.73–1.77)	0.58	1.25 (0.78–1.99)	0.35
2001–2005	0.81 (0.54–1.20)	0.29	0.71 (0.48–1.06)	0.09	1.06 (0.70–1.61)	0.77
2006–2010	0.66 (0.44–1.00)	0.05	0.55 (0.37–0.83)	0.004[b]	1.04 (0.68–1.60)	0.85

Abbreviations: AEDs = antiepileptic drugs; CI = confidence interval; HR = hazard ratio; ND = neurodevelopmental; ref. = reference group.
[a] Cox proportional hazards models. Increase in HR means shorter time to event compared with reference group. Dependent variables (in separate models) = time to surgery, time to referral, or time from referral to surgery. Independent variables for all models include clinical, diagnostic, and demographic variables as described above, all adjusted for year of cohort. Missing data for seizure frequency (n = 6); operation type (n = 7); etiology (n = 26); number of AEDs (n = 18); race/ethnicity (n = 2); and insurance type (n = 10).
[b] Statistical significance of $p \leq 0.05$.

whites with Medicaid (time to surgery and to referral) and compared with Hispanics with Medicaid (time to surgery; figure 1). This finding was observed concomitant with an increase in the proportion of Hispanic children having surgery at UCLA, with the largest increase since 2000 (figure 2).

We investigated whether the associations of having a pre-referral MRI with shorter times to referral, surgery, and referral to surgery were attributable to having the test or to an abnormal result. We found that children who had an MRI before referral had a shorter time to surgery compared with those without an MRI regardless of whether the MRI was normal (HR 1.67, 95% CI 1.16–2.40) or abnormal (HR 2.03, 95% CI 1.52–2.71; table e-3). A similar finding was seen for time to referral. Children who had an abnormal pre-referral MRI had a shorter time from

referral to surgery compared with children without an MRI (HR 1.51, 95% CI 1.12–2.03; table e-3). Older age of epilepsy onset was no longer associated with a shorter time to surgery or to referral in sensitivity analyses excluding children older than 10 years at epilepsy onset.

DISCUSSION In a large cohort from a single institution in southern California, we found that shorter times from epilepsy onset to pediatric epilepsy surgery were associated with clinical severity including history of IS and seizure frequency (daily or more), and with sociodemographic factors such as having private insurance and Hispanic ethnicity and having had a brain MRI before referral irrespective of whether the imaging was positive for an epileptogenic lesion. We did not find an association of time to surgery with

Table 3 Times to referral and surgery (years) by race and insurance status (n = 389)[a]

	Private insurance		Medicaid/CCS		
	White (n = 275)	Hispanic (n = 35)	White (n = 32)	Hispanic (n = 47)	Log-rank p
Time to surgery					0.049
Mean (SD)	4.13 (3.69)	3.31 (2.93)	5.92 (4.04)	4.99 (3.93)	
Median (IQR)	2.75 (1.27–6.00)	2.72 (1.07–5.00)	5.83 (1.50–8.75)	4.65 (1.25–7.83)	
Time to referral					0.097
Mean (SD)	3.02 (3.28)	2.46 (2.67)	4.49 (3.79)	3.73 (3.74)	
Median (IQR)	1.80 (0.60–4.20)	1.40 (0.60–3.37)	4.50 (1.09–7.30)	2.10 (0.50–6.70)	

Abbreviations: CCS = California Children's Services; IQR = interquartile range.
[a] n = 389 based on total sample N = 430 minus missing data (n = 12; race/ethnicity, n = 2; and insurance type, n = 10) and those of other race/ethnicity (n = 29). Log-rank test was used to test significance with time to surgery and time to referral across all 4 categories.

etiology. Furthermore, we found an interaction between ethnicity and insurance whereby the shortest time to surgery was associated with being Hispanic with private insurance compared with being Hispanic or non-Hispanic white with Medicaid.

Associations of time from epilepsy onset to surgery with having a history of IS and with insurance type were anticipated based on prior studies of pediatric epilepsy surgery patients and literature associating poorer specialty care access with having no insurance or "underinsurance."[9,16,18] The associations of shorter time to surgery with prior MRI and with Hispanic ethnicity were previously unknown and unexpected. Even in the literature on adult epilepsy surgery, meta-analyses of predictors of outcome have focused on clinical variables, sex, and age.[15,19] Our study was able to probe additional sociodemographic factors as well as pre-referral diagnostic testing because of the range of variables available through record abstraction.
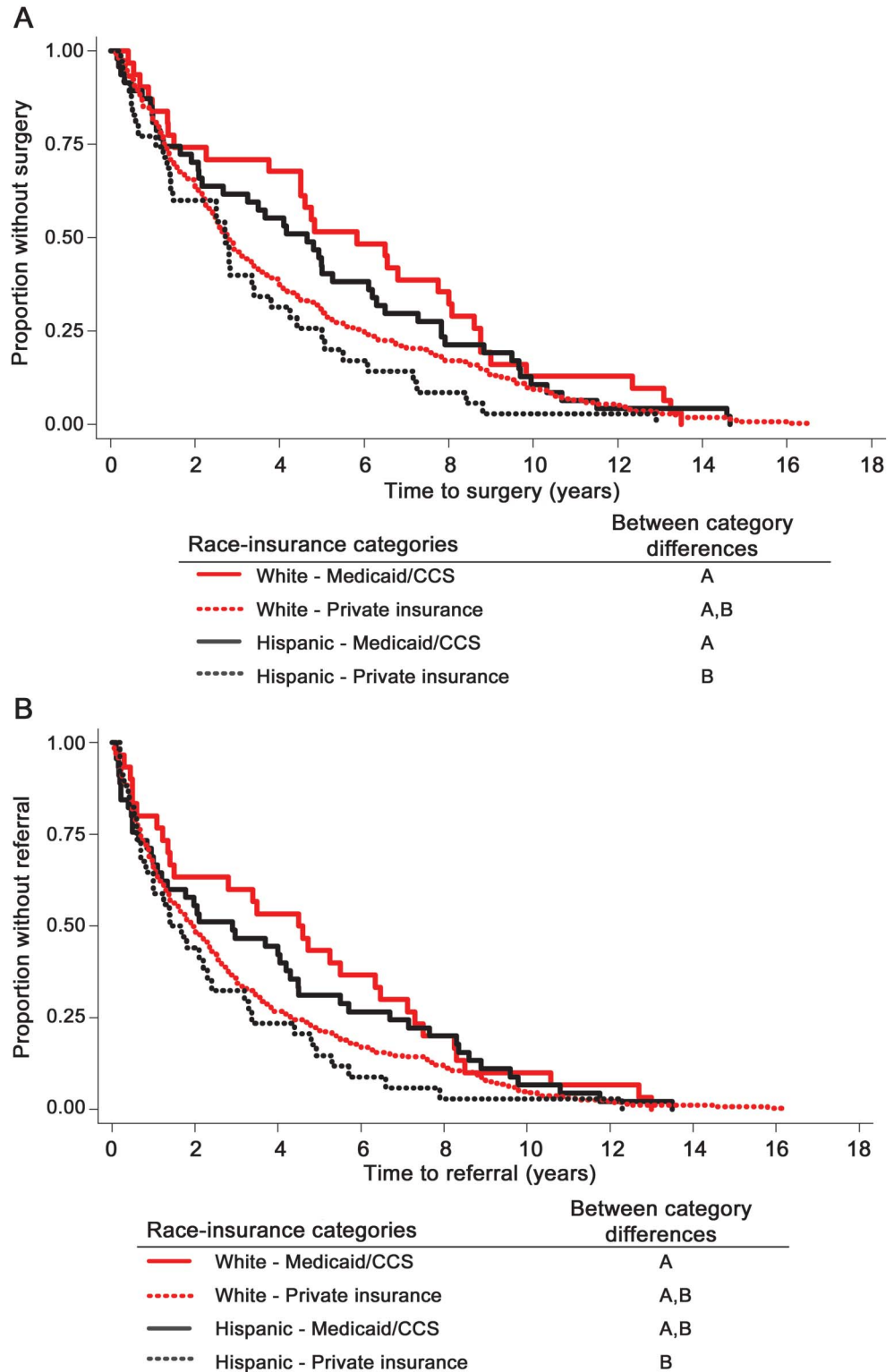
Epilepsy surgery in children differs from adults in several ways. The etiologies and operations are more heterogeneous, with cortical dysplasia and tumor being the most common, and mesial temporal sclerosis occurring less frequently in children.[6,11] Young children and infants with "catastrophic" epilepsy are at highest risk for epilepsy-induced developmental encephalopathy, and early surgical intervention may be critical in ameliorating adverse developmental outcomes, particularly given the neuroplasticity of young brains.[1,3,9] Although the natural history of mesial temporal sclerosis often includes a "quiescent period," potentially contributing to the observed 20-year epilepsy duration before adult surgery, hippocampal sclerosis accounts for a small proportion of pediatric epilepsy procedures.[20] Unlike adults, children with intellectual disability, psychiatric disease, and those of very young age are potential surgical candidates suggesting, hypothetically, that there are fewer barriers to referral for pediatric epilepsy surgery.[21]

Similar to a previous study from our group, a history of IS was strongly associated with shorter intervals to surgical treatment.[9] We note that mean time to surgery for the IS group of 2.6 years (median 1.41 years) may still be perceived as too long although more definitive evidence is needed regarding the impact of time to surgery on developmental and quality-of-life outcomes.

We found that having had a brain MRI before referral, and not what the MRI showed, was associated with shorter intervals from epilepsy onset to referral and to surgery. It is possible that having an MRI is a proxy for unmeasured factors, such as the referring physician type and knowledge about epilepsy and surgical treatment options, and parents' knowledge and advocacy for obtaining testing and for identifying treatment options.[22–25] The number of AEDs at the time of surgery may similarly be a proxy for referring physician knowledge given our finding that children taking 2 AEDs compared with 0 to 1 had longer times to referral. Limited provider knowledge regarding caring for patients with epilepsy may mediate referral delays.[26–30] In a survey of Michigan neurologists, nearly 20% reported that patients had to fail all AEDs to be considered medication refractory.[26] Another study found that 39% of adults who had epilepsy surgery at a university center came self-referred without having discussed surgery with their neurologists, and 14% were specifically told by their provider not to consider surgery.[27] In a separate study, only a small proportion of primary care providers report feeling very comfortable caring for patients with epilepsy.[30]

In the United States, lack of insurance or Medicaid insurance is more common among socioeconomically disadvantaged minority groups. In adults, there is evidence suggesting that African Americans and Hispanics are less likely to undergo temporal lobectomy compared with non-Hispanic whites.[14,17,31] Conversely, a retrospective study using the Kids' Inpatient Database found that African American children with temporal lobe

A

Race-insurance categories	Between category differences
White - Medicaid/CCS	A
White - Private insurance	A,B
Hispanic - Medicaid/CCS	A
Hispanic - Private insurance	B

B

Race-insurance categories	Between category differences
White - Medicaid/CCS	A
White - Private insurance	A,B
Hispanic - Medicaid/CCS	A,B
Hispanic - Private insurance	B

Race-insurance categories with different letters are significantly different from one another using Cox proportional hazards test. Log-rank test across all 4 categories for (A) time to surgery ($p = 0.049$) and (B) time to referral ($p = 0.097$); n = 389 based on total sample N = 430 minus missing data (n = 12; race/ethnicity, n = 2; and insurance type, n = 10) and those of other race/ethnicity (n = 29). CCS = California Children's Services.

Figure 2 Number of children who had epilepsy surgery by year and race at University of California, Los Angeles (UCLA) (1986–2010)
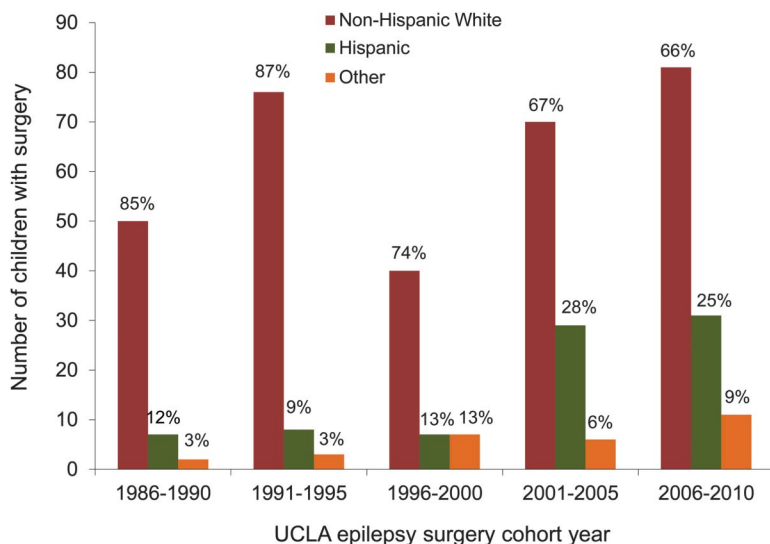
Percentages represent percent of the total number of children having surgery within each 5-year cohort period.

epilepsy were no less likely to receive temporal lobectomy than non–African American children.[16] Although we have no data on those who were eligible for surgery but not referred, we expected and found that the California equivalent of Medicaid was associated with longer intervals to surgery than private insurance. We did not anticipate that Hispanic ethnicity would be associated with shorter intervals relative to non-Hispanic whites, even after accounting for insurance type. We explored whether this finding was mediated by the higher likelihood of Hispanic patients living locally, but that only minimally attenuated the magnitude of the association of ethnicity and time to surgery. Given the increase in the number of Hispanic children who had surgery over the last decade at UCLA, regional outreach may account for the higher number and the shorter times to surgery. Furthermore, we cannot rule out the possibility that these unexpected findings may be attributable to providers who tended to care for and refer children of Hispanic ethnicity to UCLA. We are currently conducting interviews with Hispanic and non-Hispanic parents to assess referring physician type, parental level of education and employment, epilepsy knowledge, the impact of advocacy groups and social media, and other factors that contribute to patient referral for pediatric epilepsy surgery.

Regarding limitations, our analysis was limited to 1 pediatric epilepsy center having a relatively higher proportion of younger patients, more cases of cerebral hemispherectomy, and fewer temporal lobe resections compared with other cohorts.[7,11,32–36] Nonetheless, this is one of the largest and longest followed pediatric epilepsy surgery cohorts. This region serves a very large and ethnically diverse US region, allowing us to meaningfully explore both clinical and nonclinical factors among Hispanic children. Additionally, the exact timing of medical intractability was not available from our data sources. Furthermore, our sample is limited to those children who underwent surgery; we have no data on children who were referred but to whom surgery was declined. Because we do not have data on children who were never referred, including those who may have been uninsured, we cannot directly address access to care.

For parents of children with epilepsy, pediatricians, and general neurologists, this study identified not only clinical severity (spasms and greater seizure frequency) but also pre-referral diagnostic imaging, private insurance, and Hispanic ethnicity as factors associated with shorter time from epilepsy onset to surgery for pediatric epilepsy surgery patients. Although our results need to be substantiated with prospective, multicenter studies, our findings highlight the need for standardized protocols regarding prompt timing of referral of children with medically refractory epilepsy to specialty care, and underscore the importance of the development of clinical interventions, in addition to policy and advocacy strategies to remediate such delays.

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Editor's Note to Authors and Readers: Levels of Evidence in *Neurology*®

Effective January 15, 2009, authors submitting Articles or Clinical/Scientific Notes to *Neurology*® that report on clinical therapeutic studies must state the study type, the primary research question(s), and the classification of level of evidence assigned to each question based on the classification scheme requirements shown below (left). While the authors will initially assign a level of evidence, the final level will be adjudicated by an independent team prior to publication. Ultimately, these levels can be translated into classes of recommendations for clinical care, as shown below (right). For more information, please access the articles and the editorial on the use of classification of levels of evidence published in *Neurology*.[1-3]

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Classification scheme requirements for therapeutic questions

Class I. A randomized, controlled clinical trial of the intervention of interest with masked or objective outcome assessment, in a representative population. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences.

Class II. A randomized, controlled clinical trial of the intervention of interest in a representative population with masked or objective outcome assessment that lacks one criterion a-e in Class I or a prospective matched cohort study with masked or objective outcome assessment in a representative population that meets b-e in Class I. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences.

Class III. All other controlled trials (including well-defined natural history controls or patients serving as their own controls) in a representative population where outcome is independently assessed or independently derived by objective outcome measurements.

Class IV. Studies not meeting Class I, II, or III criteria including consensus or expert opinion.

AAN classification of recommendations

A = Established as effective, ineffective, or harmful (or established as useful/predictive or not useful/predictive) for the given condition in the specific population. (Level A rating requires at least two consistent Class I studies.)

B = Probably effective, ineffective, or harmful (or probably useful/predictive or not useful/predictive) for the given condition in the specific population. (Level B rating requires at least one Class I study or two consistent Class II studies.)

C = Possibly effective, ineffective, or harmful (or possibly useful/predictive or not useful/predictive) for the given condition in the specific population. (Level C rating requires at least one Class II study or two consistent Class III studies.)

U = Data inadequate or conflicting; given current knowledge, treatment (test, predictor) is unproven.