Neurology Asia 2021; 26(3) : 509 – 520

Evaluation and outcomes of paediatric epilepsy surgery in Singapore: A single-centre audit

[1]Si Qi Tan *BSc MD*, [2]Adeline Seow Fen Ngoh *MBBS MRCPCH*, [3]Wai Hoe Ng *MD FRACS*, [4]Wanying Xie *FRCR MMed*, [2]Janardhan Krishnappa *MBBS MRCPCH*, [1]Nazima Binte Sahul Hamed *BSc*, [5]Phua Hwee Tang *FRCR MMed*, [6]Tchoyoson Choie Cheio Lim *FRCR MMed*, [7]Kenneth Tou En Chang *MBChB, FRCPath*, [8]Ming Lee *MBChB*, [9]Martha I-Ming Kao *BHSc (Nurs) Grad Dip (Nurs)*, [3,10]David Chyi Yeu Low *MRCS FRCSEd(SN)*, [2]Derrick Wei Shih Chan *BMBS MRCPCH*

[1]Department of Paediatrics, KK Women's and Children's Hospital; [2]Department of Neurology, KK Women's and Children's Hospital; [3]Department of Neurosurgery, National Neuroscience Institute; [4]Department of Nuclear Medicine and Molecular Imaging, Singapore General Hospital; [5]Department of Diagnostic and Interventional Imaging, KK Women's and Children's Hospital; [6]Department of Neuroradiology, National Neuroscience Institute; [7]Department of Pathology and Laboratory Medicine, KK Women's and Children's Hospital; [8]Department of Pathology, Singapore General Hospital; [9]Nursing Clinical Services - Neurology, KK Women's and Children's Hospital; [10]Department of Neurosurgery, KK Women's and Children's Hospital, Singapore

Abstract

Background: Paediatric epilepsy surgery reduces seizure burden in drug-refractory epilepsy reducing long-term neurocognitive damage. *Methods:* Single-centre retrospective audit of pre-surgical evaluations and outcomes of the paediatric epilepsy and epilepsy surgery programme over eleven years at KK Women's and Children's Hospital, Singapore. Data were collected based on National Institute of Neurological Disorders and Stroke Common Data Elements guidelines. Outcome was categorized using Engel classification scale, and favourable outcome defined as greater than 50% decrease in seizure frequency or drop attacks. *Results:* Thirty-three children underwent epilepsy surgery, with mean follow-up 3.8±3.1 years. Median age at surgery was 10.9 years. Twenty-four children with focal epilepsy underwent resection of the epileptogenic focus, including lesionectomy (*n=8*), anterior temporal lobectomy (*n=7*), extratemporal lobectomy (*n=7*) and hemispherectomy (*n=2*). Nine children underwent corpus callosotomy for Lennox Gastaut Syndrome (*n=8*) and West Syndrome (*n=1*). Median hospital stay duration was ten days. All twenty-three focal epilepsy patients with minimum three-month follow-up achieved greater than 50% seizure reduction. Fifteen (65%) focal epilepsy patients achieved seizure-freedom (Engel Class IA) after first surgeries. Four patients required second surgeries, with two achieving seizure-freedom. Intraoperative MRI (iMRI) is beneficial. All nine corpus callosotomy patients (100%) achieved greater than 50% decrease in drop attacks. Number of antiepileptic drugs was weaned for 21/32 (66%) patients. Post-operative complications were low and some patients had anticipated neurological deficits. Outcomes were comparable to current literature.
Conclusions: In well-selected candidates with tailored evaluation, paediatric epilepsy surgery is a safe therapeutic option with favourable outcomes and can be performed across the entire paediatric age range.

Keywords: Drug-refractory epilepsy, Epilepsy surgery, Focal epilepsy, Paediatric epilepsy

INTRODUCTION

Poorly-controlled epilepsy in children is detrimental to the developing brain.[1] One third of children with epilepsy have drug-refractory epilepsy (DRE)[2,3], defined as poor seizure control despite trials of two tolerated, appropriately chosen and used antiepileptic drugs (AED).[4] In paediatric focal epilepsy, DRE is particularly common, especially if an epileptogenic lesion is identified on neuroimaging[5,6] and only 32.7% with abnormal neuroimaging achieve spontaneous remission, defined as five years seizure- and

Address correspondence to: Tan Si Qi, KK Women's and Children's Hospital, 100 Bukit Timah Rd, Singapore 229899. Tel (65) 9126 4282, Email: siqi.tan@mohh.com.sg

Date of Submission: 4 February 2021; Date of Acceptance: 8 June 2021

https://doi.org/10.54029/2021zpd

medication-free[10]. Epilepsy surgery is currently the only cure in focal DRE.[7-9] Randomized controlled trials of epilepsy surgery in adult temporal lobe epilepsy and paediatric focal epilepsy showed 58% seizure-freedom versus 8% treated medically[11] and 77% seizure-freedom versus 6% treated medically[12] respectively. Early epilepsy surgery improves rehabilitation potential, prevents further developmental damage and is more cost-effective long term[8,10,12] but is under-utilized.[13]

Epilepsy surgeries can be curative or palliative. Curative surgery includes lesionectomy, temporal or extratemporal lobectomy, hemispherotomy, in which the epileptogenic zone is neurologically disconnected but left intact, or hemispherectomy. Palliative surgery aims to reduce seizure burden and negative sequelae and includes corpus callosotomy, to disrupt interhemispheric seizure spread thereby decreasing drop attacks that otherwise cause falls and trauma[14], and Vagus Nerve Stimulator (VNS) implantation.

We audited paediatric epilepsy surgeries performed KK Women's and Children's Hospital (KKH) in Singapore, pre-surgical evaluation and surgical outcomes.

METHODS

Study settings and patient selection

We audited all drug-refractory epilepsy (DRE) patients who underwent epilepsy surgery at KK Women's and Children's Hospital in Singapore between January 2009 and October 2020.

Demographics, age of seizure onset, school status, age at time of surgery, and relevant medical histories were collected from patient records. Seizure semiology was recorded from clinical history and electroencephalogram (EEG) reports and categorized according to the 2017 ILAE seizure and epilepsy syndrome classification.[15] Participant and disease characteristics, neuroimaging, EEG, surgery and pathology data were classified in accordance with the National Institute of Neurological Disorders and Stroke Common Data Elements guidelines for epidemiologic studies of epilepsy.[16] Confidentiality was maintained according to institutional regulations. Ethics approval was not required as this study was an institutional audit.

Pre-surgical evaluation and selection for surgery

All patients had undergone investigation with continuous video EEG and magnetic resonance imaging (MRI). Interictal and ictal epileptiform discharges were classified concordant if ≥75% of discharges corresponded to predicted seizure focus. In patients with multiple seizure types the most common seizure was analysed.

Selected patients with unclear localization on EEG or lesion-negative MRI scans underwent 18F-Fluorodeoxyglucose (FDG) position emission tomography (PET) scans to localize epileptogenic zones. In patients whose resection plan potentially included eloquent cortex, functional magnetic resonance imaging (fMRI) was performed to evaluate motor and language function to predict post-operative deficits. Patients of school age also underwent neuropsychological evaluation. Suitable candidates for resective or palliative surgery were counselled by the paediatric epileptologist and paediatric neurosurgeon, with pre-surgical planning performed jointly.

Surgical approach and histological classification

Operative findings and extent of resection were obtained from records and post-operative imaging. Surgical resection included standard temporal lobectomy, tailored lobectomies, lesionectomies, anatomical hemispherectomy, and corpus callosotomies. Where possible, intra-operative MRI (iMRI) was used to guide resection. Intraoperative electrocorticography (ECoG) was also utilized in selected cases to further delineate the epileptogenic zone. In all cases the epileptologist and epilepsy neurosurgeon confirmed the resection plan pre-operatively, evaluated the extent of resection intra-operatively (with use of ECoG and iMRI scans where indicated or available) and determined the resection margins together, balancing resection extent to optimize seizure control and minimize deficits.

Histological classification was extracted from clinical histopathology reports. FCD was categorized according to the recent ILAE classification scheme.[17] Other pathological findings and tumour subtypes were described based on World Health Organization classification.[18]

Surgical outcomes

Post-operative complications were classified into (1) minor reversible medical complications such as metabolic disturbances, post-operative fever, cerebrospinal fluid leak, infections, aseptic meningitis, and intracranial hematomas, (2) minor neurological complications such as post-operative seizures or transient neurological deficits resolving within three months, and (3) major medical and neurological complications such as hydrocephalus

or abscesses requiring intervention, or unexpected neurological deficits persisting beyond three months. Length of hospital stay and need for re-operation were also recorded.

Outcome was recorded based on the last paediatric neurologist consult and categorized using the Engel classification system.[19] Patients with minimum three months follow-up were included in outcome analysis. Favourable outcome was defined as greater than 50% decrease in frequency of seizures or drop attacks. Post-operative AEDs, date of seizure recurrence, and qualitative descriptions were also recorded.

Statistical analyses

Descriptive statistical analyses were performed using Microsoft Excel.

RESULTS

Patient demographics and baseline characteristics

Thirty-three patients (19 males, 14 females) with DRE underwent epilepsy surgery - Chinese (*n*=20, 61%), Malay (*n*=8, 24%), Indian (*n*=1, 3%) and others (*n*=4, 12%). Thirty-two (97%) had minimum of three months post-surgical outpatient follow-up (mean 3.9±3.1 years). Mean age was 3.4±4.6 years (range 8 hours of life-16 years) at seizure onset and 10.2±6.5 years (range 3 months-25 years) at surgical evaluation. Mean duration of epilepsy prior to operation was 7.2±6.4 years (range 11 days-24 years). Mean age of surgery was 10.6±6.7 years (range 5 months-25 years, median 10.9 years).

Most (24/33 (73%)) had focal epilepsy: eight temporal lobe (24%), six frontal lobe (18%), four occipital lobe (12%), two parieto-occipital (6%), one parietal lobe (3%) and four hemispheric (12%). Eight (24%) had Lennox-Gastaut syndrome (LGS) and two (6%) had West Syndrome (WS). Five (15%) had associated underlying diagnoses: three Tuberous Sclerosis (TS), one Sturge-Weber Syndrome (SWS) and one FCD with Sodium Voltage-Gated Channel Alpha Subunit 1 (*SCN1A*) mutation.

Clinical phenotype and epilepsy diagnoses are listed in Table 1 and Supplementary Table 1. Seizure frequency ranged from once a year (in a patient with high probability of cure with epilepsy surgery) to refractory status epilepticus. Sixteen (48%) had global developmental delay, and twelve (36%) were cognitively or language delayed. Seventeen (51%) patients had abnormal neurological examination pre-operatively, and six (18%) exhibited behavioural difficulties with autistic features. Twelve (36%) attended normal school, 12 (36%) attended special school, one (3%) was home-schooled, one (3%) attended preschool and seven (21%) were infants and pre-schoolers.

Patients trialled a mean of five AEDs prior to surgery. Four had used the ketogenic diet but did not tolerate it or showed no benefit.

Pre-surgical evaluations

Table 1 and Supplementary Table 2 included pre-surgical radiological and EEG evaluations. Ten patients (30%) had 18F-FDG PET scans performed, with 8 showing interictal focal hypometabolism and 2 showing focal hypermetabolism over the epileptogenic foci. The latter two had electrographic seizures on pre-PET EEG and were classified as ictal. Seven patients (21%) had language fMRI. An example of pre-surgical evaluation is illustrated in Figure 1.

The most common aetiology was structural (76%); 14 (42%) focal cortical dysplasia (FCD), two (6%) mesial temporal sclerosis, five (15%) ganglioglioma, oligodendroglioma or dysembryoplastic neuroepithelial tumour (DNET), three (12%) TS tubers (12%), one (4%) SWS (4%), and one with inflammation (4%) (Figure 2). In the focal epilepsy group, 22/24 (92%) had congruent lesions on MRI.

Eight patients had LGS and two had WS, with all undergoing corpus callosotomy except for one WS patient who had hemimegalencephaly and underwent hemispherectomy. Seventeen patients underwent VNS implantation and are not described further here.

In focal epilepsy patients, EEG interictal discharges lateralized to the seizure focus in 21/24 (88%) (Table 1). Ictal EEG in all 24 were localizing, with five (20%) having secondary generalization. EEG in patients with WS and LGS were consistent with the clinical syndrome, with electroclinical seizures captured in 6/8 (75%).

Epilepsy surgeries performed

Epilepsy surgery (*n*=33) comprised eight lesionectomies (24%), seven anterior temporal lobectomies with amygdalohippocampectomy (21%), four unilobar extratemporal lobectomies (16%), three multilobar extratemporal lobectomies (9%), two hemispherectomies (6%) and nine corpus callosotomies (27%). Of these surgeries (*n*=33), nine (27%) utilized iMRI and five (15%) utilized ECoG.

Table 1: Pre-operative evaluation and outcomes of paediatric patients who underwent epilepsy surgery at KKH from 2009-2020, *n*=33

Patient Number	Sex	Age of Seizure onset	Duration of Seizure (Years)	Age at surgery	Diagnosis	MRI Lesion	PET Lesion	fMRI Results	EEG Ictal Onset Location	Congruent?	Surgical Procedure	Histopathology	Seizure Control	50% Reduction? First → Second surgery	AEDs weaned down	Engel Class	Follow-up (Years)
1	F	3y5m	9.2	12y7m	Right Frontal lobe Epilepsy Tuberous Sclerosis Congenital myotonia (*CLCN1* mutation)	R inferofrontal lesion, cortical tubers (Multiple bilateral T2W hyperintense white matter lesions)	R inferofrontal hypometabolism	Language: L dominance	F3 F4	Yes	Right basifrontal lesionectomy with iMRI	Tuberous Sclerosis, FCD Type 2a	1x/day → 0	Yes	Yes	IA	4.2
2	M	3y5m	13.2	16y7m	Right Temporal lobe epilepsy with mesial temporal sclerosis, Posterior reversible encephalopathy syndrome (PRES) from Nephrotic Syndrome	R mesial temporal sclerosis (T2W white matter hyperintensity with loss of hippocampal architecture)	R mesial temporal hypometabolism	Language: L dominance	F8	Yes	Right anterior temporal lobectomy	FCD Type 3	2-3x/month → 0	Yes	Yes	IA	5.5
3	F	5y10m	0.5	6y3m	Right Hemispheric Epilepsy	R parietal Focal cortical dysplasia (T2W white matter hyperintensity, cortical thickening with decreased grey-white matter distinction)	Bilateral frontal, insular, basal ganglia, thalami, mesial temporal (R>L) hypermetabolism	-	F8	Yes	1) Right insular, frontal and temporal cortical resection with ECoG 2) Right hemispherectomy	FCD Type 2b	Every 1-2 min → every 1-2 min 2nd surgery → 0	No → Yes	Yes	IA	0.9
4	M	6m	0.5	1y	Left Hemispheric Epilepsy Hemimegaencephaly, West syndrome	L Hemimegaencephaly (Left hemisphere hyperplasia, agenesis of corpus callosum)	L Hemisphere hypometabolism	-	L hemisphere	Yes	1) Left hemispherotomy 2) Left hemispherectomy with iMRI	FCD Type 2a	10-20x/day → to 5-8x/day 2nd surgery → 0 for 2 years, then 2x/week	Yes → Yes	Yes	IIIA	7.5
5	M	7m	16.2	16y8m	Right Temporal lobe Epilepsy Tuberous Sclerosis	R parietal, temporal cortical tubers (Multiple bilateral T2W hyperintense white matter lesions)	R frontal, parietal, temporal hypometabolism	-	C4-T4	Yes	1) Right anterior temporal lobectomy and amygdalohippocampectomy 2) Right temporal lobectomy and hippocampectomy	Tuberous Sclerosis, FCD Type 2b	2-3x/week → 5-6x/day 2nd surgery → once every 7-10 days	No → Yes	No	IIIA	5.4
6	F	15y10m	6.9	22y4m	Left Frontal lobe Epilepsy	L frontal Focal cortical dysplasia (T2W white matter hyperintensity)	L frontotemporal hypometabolism	Language: L dominance	F7 C3 T3 P3	Yes	Left frontal lobectomy with ECoG	FCD Type 2b	3-6x/month → Once every 2 months	Yes	Yes	IIIA	6.6
7	F	2y0m	8.2	10y	(1) Right Frontal lobe Epilepsy (2) Right Hemispheric Epilepsy*	Non-lesional (Subtle slightly T2W hyperintensity, decreased grey-white matter distinction)	R frontal, parietal, temporal hypometabolism	-	A (Fearfulness): T3-P3 B (tonic): F4-T4, Fp2-F8	Yes (MRI-ve, PET+ve)	1) Right frontal lobectomy with ECoG 2) Right hemispherectomy with iMRI	FCD Type 2b	1-2x/week → 4-5x/per day 2nd surgery → 0	No → Yes	Yes	1A	8.9
8	F	1y	8.7	9y8m	Right Temporal lobe Epilepsy Ganglioglioma	R temporal Ganglioglioma (1.5 cm x 0.7 cm T2W hyperintensity)	-	-	T6	Yes	Right anterior temporal lobectomy and right temporal tumour resection	Ganglioglioma	10x/day → 0	Yes	Yes	IA	7
9	F	20 day	0.5	6m	Left Hemispheric Epilepsy	L fronto-parietal Focal cortical dysplasia (T2W white matter hypointensity, cortical thickening with decreased grey-white matter distinction)	-	-	Fp1-F7, F3-C3, C3-P3, C3- Cz	Yes	Left hemispherectomy	FCD Type 2b	1-13x/day → 0	Yes	Yes	IA	5.1
10	M	1y	1.3	1y4m	Right Parieto-occipital Epilepsy	R parieto-occipital Focal cortical dysplasia (R occipital horn tip nodular heterotopia, grey matter dysplasia)	-	-	T4	Yes	Right parietal lesionectomy with iMRI	FCD Type 2a	10-30x/day → 2-3x/day	Yes	No	IIIA	2.4
11	F	2m	21.2	21y3m	Right Temporal-occipital Epilepsy Sturge-Weber Syndrome	Sturge Weber (R temporal, occipital lobe atrophy, calcifications and vascular malformation, enlarged choroid plexus, prominent draining veins)	-	-	Right temporo-parietal, T4-T6	Yes	Right temporo-parieto-occipital lobectomy with iMRI	Sturge-Weber Syndrome	3-4x/year→ 0	Yes	Yes	IA	1.4
12	M	2m	17.2	17y5m	Left Frontal lobe Epilepsy	L superofrontal Focal cortical dysplasia (T2W white matter hyperintensity, cortical thickening with decreased grey-white matter distinction)	L superior temporal, L amigdala hypometabolism. No frontal metabolic abnormality	Language: R dominance	F3, C3	Yes	Left frontal lesionectomy	FCD type 2b	1x/month → 2 seizures/year (provoked)	Yes	No	IIA	1.5
13	F	6m	7.8	8y4m	Right Occipital lobe Epilepsy	Non-lesional	R occipital, R inferioparietal hypermetabolism	-	PO8	Yes (MRI-ve, PET+ve)	Right occipital lobectomy	Gliosis	2-3x/day → 0	Yes	No	IA	1.3
14	M	1y10m	5.2	7y	Left Temporal lobe Epilepsy Dysembryoplastic neuroepithelial tumour (DNET)	L temporal Ganglioglioma (2.0 cm x 1.9 cm heterogeneous T2W hyperintense lesion with cystic change)	-	-	T3-T5	Yes	Left temporal lobectomy with ECoG	DNET	1-2x/week → 0	Yes	Yes	IA	1

15	M	13y7m	2.5	16y	Right Occipital lobe Epilepsy Ganglioglioma	R medial occipital DNET (2.2 cm x 2.1 cm T2W hyperintense lesion with cystic change)	-	-	O2	Yes	Right occipital lobectomy and right occipital tumour resection	Ganglioglioma	5x/year→ 0	Yes	Yes	IA	6.8
16	F	3y	0.5	3y6m	Right Frontal lobe Epilepsy	R frontal Focal cortical dysplasia (T2W white matter hyperintensity, cortical thickening)	-	-	Right frontal	Yes	Right frontal lesionectomy	FCD type 2b	50-150x/day → 0	Yes	No	IA	0.8
17	F	10m	2.1	2y10m	Left Temporal lobe epilepsy Oligodendroglioma	L temporal Focal cortical dysplasia (T2W white matter hyperintensity, cortical thickening, loss of hippocampal architecture)	-	-	T3-T5	Yes	Left temporal lobectomy	Oligodendroglioma	3-10x/day → 0	Yes	Yes	IA	0.5
18	F	4y8m	10 days	4y8m	Meningoencephalitis with suprarefractory focal temporal lobe epilepsy	R temporal and R parietal Restricted diffusion, T2W/FLAIR hyperintensity	-	-	F8-T4-T6, C4	Yes	Right temporal lobectomy with tailored resection with ECoG	Meningoencephalitis	Suprarefractory status epilepticus (Not included in outcome as transferred care to other institution)	-	-	-	-
19	M	9y	3	12y	Left Parietal lobe epilepsy Ganglioglioma	L parieto-occipito-temporal Ganglioglioma (3.3 x 3.7 cm lobulated cystic T2W hyperintense lesion)	-	-	P3, T5	Yes	Left parietal lesionectomy	Ganglioglioma	4 times over 3 years → 0	Yes	No	IA	0.7
20	M	2m	5.4	5y5m	Right Frontal lobe epilepsy	R fronto-parietal Focal cortical dysplasia (T2W white matter hypointensity, cortical thickening, decreased grey-white matter distinction	-	Motor: R dominance	C3, P4	Yes	Right frontal lesionectomy with iMRI	FCD type 2a	Daily → 1-2 times a night few seconds	Yes	No	IIA	0.8
21	M	8 hours of life	0.5	5m21d	Right Occipital lobe epilepsy Neuronal migration disorder (*SCN1A* mutation)	R parieto-occipito-temporal Focal cortical dysplasia (Cortical thickening, decreased grey-white matter distinction)	-	-	R posterior temporo-occipital	Yes	Right temporo-parieto-occipital lobectomy with iMRI	FCD type 2a	30-40x/day → 0	Yes	Yes	IA	0.5
22	M	16y	2.8	19y	Right Occipital lobe epilepsy DNET	R occipital DNET (2.0 x 1.7 cm T2W hyperintense lesion)	-	Activation on visual medial to right occipital lesion	O2	Yes	Right occipital lesionectomy	DNET	3-4 x/week → 0	Yes	No	1A	0.3
23	F	6m	3.1	3y8m	Right Temporal lobe epilepsy with mesial temporal sclerosis West Syndrome	R temporal Mesial temporal sclerosis (right hippocampus atrophy with mild widening of temporal horn)	-	-	Fp2-F4-F8-T4-T6	Yes	Right anterior temporal lobectomy with iMRI	Gliosis	Daily → 0	Yes	No	1A	0.25
24	F	8y	3.4	11y11m	Right Parieto-occipital Epilepsy Polymicrogyria	R parieto-temporo-occipital Polymicrogyria, cortical malformation, nodular heterotopia	R parieto-occipital hypometabolism	Language: L dominance	T4	Yes	Right posterior quadrantectomy with iMRI	Polymicrogyria	Multiple times/day → 0	Yes	Yes	IA	0.5
25	M	6y	9	15y4m	Lennox-Gastaut syndrome	Non-lesional Mild hippocampal atrophy	-	-	Diffuse	-	Total corpus callosotomy	-	Drop attacks 5x/week → no drop attacks	Yes	Yes	IIIA	9.5
26	M	2y3m	9.4	11y7m	Lennox-Gastaut syndrome	Non-lesional	-	-	Diffuse	-	Total corpus callosotomy with iMRI	-	Drop attacks 5-6x/day → no drop attacks	Yes	No	IIIA	7.8
27	M	3m	7.1	7y3m	Lennox-Gastaut syndrome	Non-lesional	-	-	Diffuse	-	Total corpus callosotomy	-	Drop attacks 5-6x/day → 1-2x/week, with one-week seizure-free intervals	Yes	Yes	IIIA	6.5
28	M	2y10m	8.1	10y10m	Lennox-Gastaut syndrome	Bilateral parietal and L frontal Foci of demyelination and cerebellar atrophy	-	-	Diffuse, L frontal	Yes	Total corpus callosotomy	-	Drop attacks 5x/day → no drop attacks	Yes	Yes	IA	6.4
29	F	6m	24.7	25y2m	Lennox-Gastaut syndrome	Non-lesional	-	-	Diffuse	-	Total corpus callosotomy	-	Drop attacks 4-5x/day → no drop attacks	Yes	No	IIIA	2.6
30	M	4m	7	7y3m	West Syndrome	Non-lesional	-	-	Diffuse	Yes	Total corpus callosotomy	-	Drop attacks 3x/week→ drop attacks 1x/week with less intensity	Yes	Yes	IIIA	2.2
31	M	8y	4.9	12y10m	Lennox-Gastaut syndrome	Non-lesional	-	-	Diffuse	-	Partial corpus callosotomy	-	Drop attacks every 5 minutes → no drop attacks	Yes	No	IVB	3.5
32	M	12y	10	11y	Lennox-Gastaut syndrome	Non-lesional	-	-	Diffuse (frontal dominant)	-	Partial corpus callosotomy with iMRI	-	Drop attacks >10x/day → no drop attacks	Yes	Yes	IIIA	8
33	M	1y	18.5	18y6m	Lennox-Gastaut syndrome Tuberous Sclerosis with SEGA	Third ventricle subependymal giant cell astrocytoma, multiple bilateral cortical tubers	-	-	Fp1 (staring) T3-T5 (drop attack), diffuse (GTC)	Yes	Partial corpus callosotomy with resection of intraventricular SEGAs	Tuberous Sclerosis with SEGA	Drop attacks several times/day→ seizures in clusters (2-5x/day) then 1 week seizure free	Yes	No	IIIA	7
														29/32 (90%) → 32/32 (100%)	21/32 (66%)		

Abbreviations: Age - m: month, y: year. Semiology - GTC: generalized tonic clonic, L: left, LL: lower limb, R: right, UL: upper limb. Diagnosis - DNET: dysembryoplastic neuroepithelial tumour, FCD: focal cortical dysplasia, LGS: Lennox-Gastaut Syndrome, SCN1A: Sodium Voltage-Gated Channel Alpha Subunit 1, SEGA: Subependymal giant cell astrocytoma, MRI terminology - FLAIR: Fluid-attenuated inversion recovery, T2W: T2-weighted, T1W: T1-weighted, EEG electrode locations- F: frontal, Fp: pre-frontal, T: temporal, P: parietal, O: occipital, C: central, Others: EEG: electroencephalography, ECoG: Electrocorticography, iMRI: intra-operative MRI.

*Patient 7 initially diagnosed as right frontal lobe epilepsy at time of surgery, subsequently right hemispheric epilepsy.

Table 2: Overview of epilepsy surgery outcomes at KK Women's and Children's Hospital from 2009-2020, *n*=32

Surgery, Pathology	Number performed at KKH, n (%)	Indications	Consistent predictors of success	Seizure Freedom Rate, literature	>50% seizure reduction Rate at KKH, n (%)	Seizure Freedom Rate at KKH, n (%)
Lesionectomy Focal Cortical Dysplasia With Tuberous Sclerosis With polymicrogyria DNET Ganglioglioma	**8 (25%)** 6 1 1 1 1	Well-defined, radiographically apparent lesions (FCD, low grade tumours, arteriovenous malformation)	- Gross total resection	60-100%	8 (100%)	5 (63%)
Anterior Temporal Lobectomy Hippocampal sclerosis Tuberous Sclerosis DNET Ganglioglioma Oligodendroglioma Gliosis	**6 (19%)** 1 1 1 1 1 1	Small lesions limited to temporal lobe (mesial temporal sclerosis, FCD, arteriovenous malformation, tuberous sclerosis)	- Visible lesion - Lack of secondary generalization - Lack of bilateral involvement	76%	5 (83%) 6 (100%) after repeat ATL	5 (83%)
Extratemporal Lobectomy (Unilobar) Focal Cortical Dysplasia Ganglioglioma Gliosis	**4 (13%)** 2 1 1	Small lesions away from temporal lobe (low-grade tumours, FCD, gliosis, tuberous sclerosis)	- Short epilepsy duration - Lesional aetiology - No secondary generalization - Ictal EEG localization - Frontal location	56%	3 (75%)*	2 (50%)
Extratemporal Lobectomy (Multilobar) Focal Cortical Dysplasia Sturge Weber Syndrome	**3 (9%)** 2 1				2 (67%)†	2 (67%)
Hemispherectomy Focal Cortical Dysplasia Hemimegaencephaly	**4‡ (13%)** 3 1	Large lesions involving majority of hemisphere (large FCD, hemi-megalencephaly)	- Acquired or progressive aetiology - Unilateral EEG involvement - No history of other resections	50-85%	3 (75%) 4 (100%) after repeat hemi-spherec-tomy	3 (75%)
Corpus callosotomy Lennox-Gastaut Syndrome With SEGA West Syndrome	**9 (28%)** 7 1 1	Pathologies that cause significant drop-attacks, non-amenable to potentially-curative resection	- Infantile spasms - Normal MRI - Short epilepsy duration - Complete callosotomy - Idiopathic aetiology	18.8% overall, 55.3% in drop attacks	9 (100%) in drop attacks	6 (67%) in drop attacks

* Patient 7 initially underwent right frontal lobectomy but did not achieve >50% reduction in seizures, hence underwent hemispherectomy, and is subsequently seizure free.

† Patient 3 initially underwent right insular, frontal and temporal cortical resection but did not achieve >50% reduction in seizures, hence underwent hemispherectomy, and is subsequently seizure free. She was hospitalized for 207 days in total. After the first multilobar resection, she still had persistent seizures, hence underwent a right hemispherectomy 152 days after. After the right hemispherectomy, she was seizure free, and underwent a period of inpatient neuro-rehabilitation. The second longest length of hospital stay was 32 days.

‡ This value includes two patients (Patient 3 and Patient 7) who proceeded with hemispherectomy as second surgeries, as seizures recurred after the first surgeries.

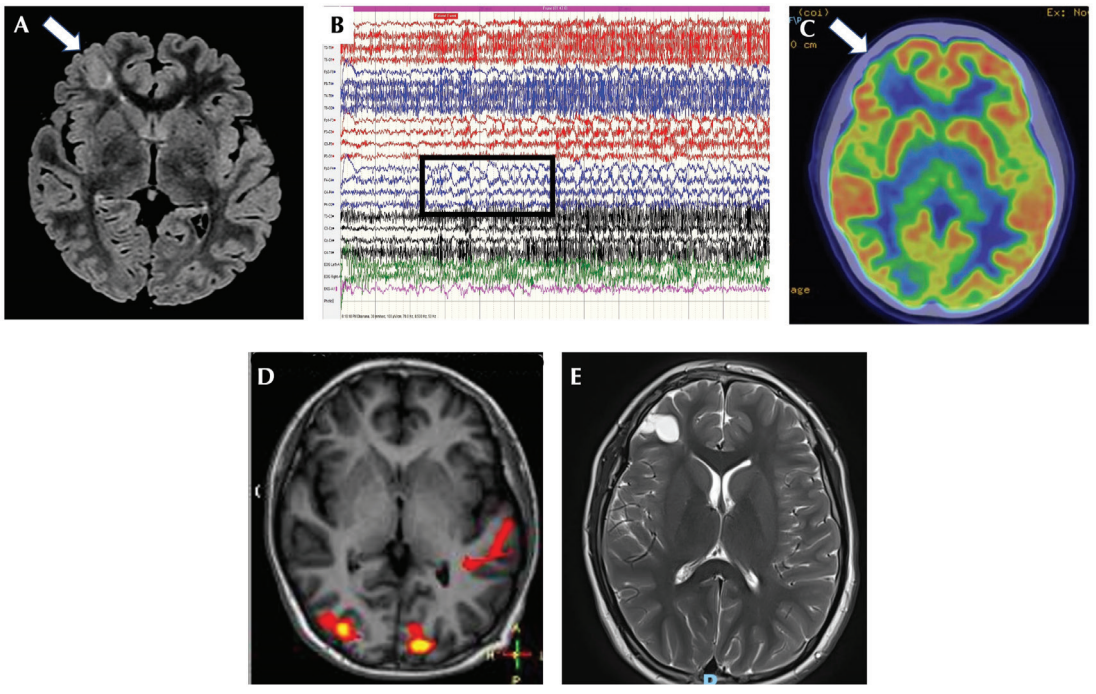

Figure 1. Pre-surgical evaluation for Patient 1.
Representative images from Patient 1, a 12-year-old with Tuberous Sclerosis who underwent lesionectomy for Right Lateral Frontal lobe epilepsy. MRI FLAIR showed a right frontal lesion (A; arrow) that corresponded with F4 discharges on EEG (B; box) and hypometabolism focus on PET (C; arrow). EEG (B) showed rhythmic 2-2.5 Hz delta activity reversing F4 and F3, spreading to involve F8, consistent with a right frontal lobe onset. Clinically, she "raised her upper limbs, turned her head to the right while abducting lower limbs". Functional MRI (colour overlays) performed for pre-surgical planning showed speech localising to the left side (D). Post-surgical T2-weighted MRI showed the excision of right frontal lobe epileptic focus (E).

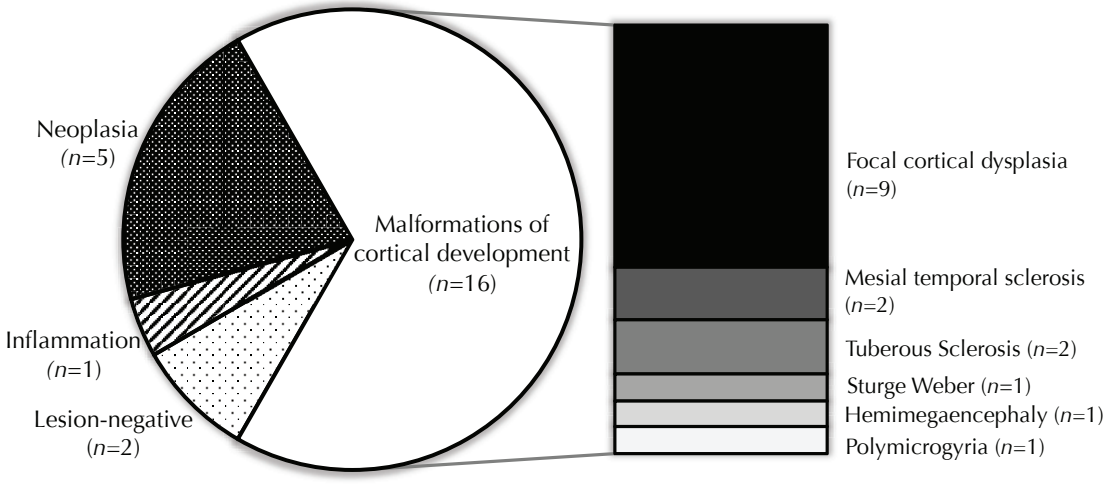

Figure 2. MRI Findings in children with refractory focal epilepsy undergoing resective surgery
Of 24 patients, the most common finding was a malformation of cortical development, followed by benign tumours and one with inflammation (Table 2, Patient 18). Two patients had lesions that were MRI-negative but PET-positive.

Histopathology in focal epilepsy patients (*n*=24) revealed 14 FCD (of which two were associated with TS lesions), three gangliolioma (one WHO Grade I, two WHO Grade II), two DNET, one oligodendroglioma, two gliosis, one showing inflammation, and one SWS malformation.

Post-operative course

Median hospital stay was ten days (range 4-207 days). Common minor complications were: electrolyte disturbances (*n*=11), post-operative fever (*n*=9), nausea and vomiting (*n*=6), culture-proven infections such as pneumonia or urinary tract infections requiring antibiotics (*n*=6), Syndrome of Inappropriate Antidiuretic Hormone secretion (SIADH) (*n*=3), AED-related extravasation (*n*=3) and rash (*n*=3). Minor neurological complications were post-operative seizures (*n*=9) and AED-related drowsiness (*n*=5).

None of the 15 patients who underwent lesionectomies or anterior temporal lobectomy had motor deficits. One occipital lesionectomy patient had an expected visual scotoma. Nine patients underwent extra-temporal unilobar or multilobar lobectomies and hemispherectomy, with eight having anticipated neurological deficits of hemiparesis, homonymous hemianopia and/or hemispatial neglect.

One patient required debridement for wound dehiscence four months post-operatively, one required evacuation of a tension pneumocephalocele on post-operative day one, one had a right parietal swelling requiring bedside aspiration on post-operative day ten, and surgical evacuation of subgaleal and epidural haematoma on post-operative day 15. One developed subdural haemorrhage and lacunar infarcts post-corpus callosotomy. There were no post-operative mortalities.

Outcome

Most patients had improved seizure control *(Table 1)*. Following first surgery, 15/23 (65%) focal epilepsy patients were seizure-free (Engel Class IA), and 2/23 (9%) have rare disabling seizures (Engel Class II). Six patients (Patients 3, 4, 5, 6, 7, 10) had seizure recurrence following surgery (Engel Class IIIA), with median time of recurrence of 51 days. Two with hemispherotomies and one with tailored cortical resection to spare motor cortex subsequently underwent anatomical hemispherectomy. Another had extended temporal lobectomy as second surgery. All four of them achieved >50% seizure reduction following second surgery, with two becoming seizure-free. Ultimately, 17/23 (74%) of focal epilepsy patients were seizure-free. Corpus callosotomy reduced drop attacks by >50% in 9/9 (100%), with 6/9 (67%) having residual seizures but no further drop attacks and 1 patient completely seizure-free. AEDs were weaned in 21/32 (66%), with 14/32 (44%) on two or fewer AEDs at the last clinic consult.

DISCUSSION

This audit demonstrates good outcomes in our paediatric epilepsy surgery programmes, comparable to published outcomes by programmes elsewhere. The 23 of 24 patients who underwent resections for focal epilepsy continued follow-up for at least three months. All 23 achieved greater than 50% seizure reduction, and 17 were seizure-free (Engel Class IA). For patients who underwent corpus callosotomies, 9/9 (100%) achieved greater than 50% decrease in drop attacks. Our outcomes were compared to published outcomes in Table 2.[20]

Concerns by patients and caregivers of serious postoperative morbidity and mortality are common and often lead to epilepsy surgery delay. However, mortality in childhood DRE is five to nine times higher than the general population.[21,22] Seizure freedom is rare in un-operated children with neuroimaging abnormalities, occurring in only 8.6% of children,[23] Anecdotal reports from our patients' caregivers also support improved quality of life and learning following successful surgery, suggesting that the risks of continued seizures outweigh risks of surgery. Early epilepsy surgery offers the possibility of reduction or discontinuation of anticonvulsants. AED discontinuation is associated with improved postoperative intelligence[24], alertness, psychomotor speed, memory and learning.[10] Most patients continue AEDs for the first six to 24 months after surgery, after which some reduce or withdraw treatment.[25] Many continue AEDs, albeit with improved seizure control, and in a report of epilepsy surgery for paediatric cerebral malformations, 75% were still taking anticonvulsants after five years[26], similar to our institution. Long-term studies do support a higher likelihood of stopping AEDs following epilepsy surgery. A longitudinal study of 60 children from Sweden reported that 86% of seizure-free children in the surgical group were off AEDs by ten years, compared to none of the non-operated patients.[26]

Temporal lobe epilepsy has a particularly favourable surgical outcome, with resection

considered the standard of care in drug-refractory cases. Of the six children in our series with sufficient follow-up, 100% were seizure-free post-surgery. This is comparable with seizure freedom rates of approximately 76% observed in other studies.[27]

Extra-temporal epilepsy is more prevalent in paediatric patients but is reported to have a lower seizure-freedom rate: 56% in a systemic review with 1259 paediatric patients.[28] Among our extra-temporal epilepsy patients, 100% achieved greater than 50% seizure reduction, with 10/17 (59%) achieving Engel Class IA outcome after first surgeries and two more achieving Engel Class IA outcome after second surgery (overall 12/17 (71%)).

Hemispherectomy is indicated for multilobar cortical dysplasia, hemimegalencephaly, acquired perinatal vascular insults, or progressive lesions such as leptomeningeal angiomas from SWS or Rasmussen's encephalitis. Reported seizure-freedom rates varied from 50-85% among paediatric patients.[20] Postoperative hemiparesis and/or homonymous hemianopsia is generally expected. For our hemispherectomy patients, 3/4 (75%) achieved Engel Class IA seizure-freedom.

DNETs and gangliogliomas are benign tumours that can be highly epileptogenic. DNETs, in particular, tend to be extremely refractory to AEDs.[29,30] All five of our patients (Patients 8, 14, 15, 19, 22) who underwent tumour resection had prior cognitive delay and had failed multiple AEDS. After surgery, all five were seizure-free, with three weaning AEDs. These figures are comparable to results from Ranger and Diosy's 2015 systematic review that demonstrated long-term seizure-freedom in 86% and seizure improvement in 99% of the 185 paediatric patients who underwent surgical resection of DNETs.[30]

Corpus callosotomy is beneficial in suitable patients, even if complete seizure freedom rates have been reported to be less than 10-20%.[20,32] We evaluated and selected patients with drop attacks amenable to surgical intervention and 6/9 (67%) achieved freedom from drop attacks, comparable to 55.3% demonstrated in a 2018 metanalysis[33]. At our institution, three corpus callosotomies performed before 2010 were partial, due to reported higher risks of transient disconnection syndrome, mutism.[9,32] From 2010, a decision was made to perform complete corpus callosotomies as we felt these are more likely to make a clinical impact. Studies have reported 88.2% worthwhile reduction in seizures for patients who had complete callosotomies compared to just 58.6% reduction in seizures for those who had partial callosotomies.[24,32,34] With this decision, we found concomitant improved seizure control. We observed no cases of disconnection syndrome or mutism and we now recommend complete corpus callosotomy to all suitable patients to optimize efficacy and avoid the need for repeat surgery.

Post-operative deficits at our centre were largely as anticipated pre-operatively. These include the one occipital lesionectomy patient with an expected visual scotoma, and the eight out of nine extra-temporal lobectomy and hemispherectomy patients who had anticipated neurological deficits of hemiparesis, homonymous hemianopia and/or hemi-spatial neglect. Post-operative complications at our centre were rare and comparable to what has previously been reported, with 4.5-5.1% having serious medical or neurological complications.[25] There were no post-operative mortalities. The four patients (12%) with unanticipated post-operative complications, such as wound dehiscence, tension pneumocephalocele or surgical related haematomas, received timely management. All four still achieved greater than 50% reduction in seizure control, and three achieved Engel Class 1A outcome ultimately. In lesionectomies and temporal lobectomies, complications resulting in permanent contralateral weakness or major visual field deficits are reported to be rare;[25] no unanticipated deficits were seen in our series.

Post-operative seizure recurrence was mainly attributed to initial conservative resection plans. The only independent factor of surgical success is complete resection of both the focal lesion and associated epileptogenic zone.[6,28,35,36] Other reasons postulated were: development of new epileptogenic zones induced by brain injury during surgery, infection, or microenvironment changes causing alterations in drug-sensitivity in pathological tissues.[37] To optimize surgical resection and reduce risks of postoperative seizures and repeat surgery, we introduced iMRI into our practice. This was especially useful for lesions that might extend beyond visible margins on MRI, or poorly defined lesions without distinct borders such as FCD or TS. iMRI use has been associated with smaller residual lesions and is protective against poor Engel outcome score.[22,25] In Sacino *et al*.'s 2016 study of 29 paediatric patients who underwent resection of FCD or heterotopia localized to eloquent cortex regions, nine of 11 patients (82%) in the iMRI resection group were seizure free (Engel Class IA) compared with seven of 18 patients (39%) in control group (p=0.05).[22] Eid *et al*.'s study also

revealed that iMRI was protective against poor seizure outcome (p=0.048) among 80 paediatric patients who underwent focal epilepsy surgery from 2003 to 2017. Additionally, this study revealed that, while iMRI may prolong mean operative time by 1.2 hours, it was not associated with additional complications.[25] In our study, seven out of 23 (30%) focal epilepsy patients had iMRI incorporated into their first surgeries. Five of these seven (71%) are now seizure free (Engel Class 1A). An example of iMRI use is presented in Figure 3. Ten out of 16 (63%) focal epilepsy patients who underwent resections without iMRI were seizure free after the first surgery. Some of these surgeries preceded introduction of iMRI, some did not require additional step of iMRI and some were unable to go for iMRI due to logistical reasons. In our experience, tailoring of resection in real time, by the epilepsy neurosurgeon and epileptologist, with iMRI offers value in limiting deficits, improving seizure outcome and reducing risk of re-operation.

One of our patients (Patient 21) harboured a pathogenic *SCN1A* mutation. He presented at eight hours of life with focal seizures characterized by eye deviation and tonic stiffening. His seizures proved refractory to several AEDs, and he had up to 30-40 seizures daily. Neuroimaging demonstrated FCD and, following tailored resection, is seizure-free and making developmental progress. Presence of genetic mutations is often taken as a contraindication to epilepsy surgery. These should be weighed up during evaluation, but detailed phenotyping should ultimately drive clinical decision-making.

Our study is limited by small sample size, which does not permit further sub-analysis. Follow-up studies of longer-term seizure control and neuropsychological and social outcomes would also be desirable.

In conclusion, the outcomes of our epilepsy surgery programme are comparable to other centres despite smaller numbers relative to centres overseas. Patients with successful surgical

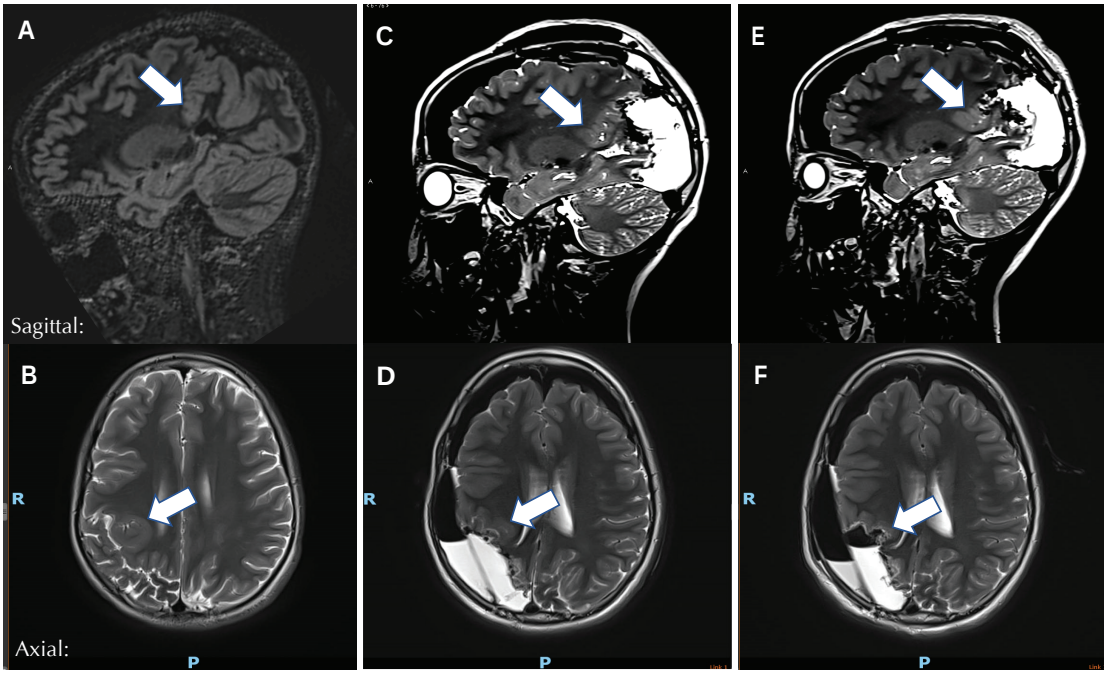

Figure 3. Right parieto-occipital lesionectomy guided by intra-operative MRI.
Patient 24 had drug-resistant focal epilepsy from right parieto-occipital polymicrogyria. Pre-operative MRI showed right parieto-occipital lobe polymicrogyria on sagittal image (A; arrow), and corresponding abnormal cortex on axial image (B; arrow). This patient underwent right parieto-occipital lesionectomy at 11 years old. The first intra-operative T2-weighted MRI showed residual abnormal cortex anterior to surgical cavity (C; arrow, D; arrow), further resection of the anterior subcortical margin was performed in the same session (E; arrow, F; arrow). Mild residual abnormal cortex was not shown to be epileptogenic using intra-operative Electrocorticography (ECoG) and decision was made to halt resection at this point so as to preserve motor function. At the six-month follow-up, this patient was seizure free.

outcome demonstrated better quality of life, concentration, mood, educational and employment opportunities. For well-selected candidates, in whom spontaneous, permanent and complete remission is otherwise rare, epilepsy surgery changes the natural course of disease. iMRI is beneficial in tailoring resection and avoiding re-operation. Patients with positive genetic findings do not have to be excluded from epilepsy surgery if electroclinical phenotype suggests this may be of benefit.

Epilepsy surgery remains an underutilized treatment for children with DRE and should be offered early in suitable patients, rather than as a last resort or not at all.[10]

ACKNOWLEDGEMENT

We would like to thank KK Women's and Children's Hospital Department of Paediatric Neurology and Prof Lim Shih Hui for their support.

DISCLOSURE

Financial support: None

Conflict of interest: None

REFERENCES

1. Baca CB, Vickrey BG, Caplan R, Vassar SD, Berg AT. Psychiatric and medical comorbidity and quality of life outcomes in childhood-onset epilepsy. *Pediatrics* 2011;128(6):e1532-1543.
2. Hauser WA. The prevalence and incidence of convulsive disorders in children. *Epilepsia* 1994;35 (Suppl 2):S1-6.
3. Chan D, Phuah H-K, Ng YL, Choong CT, Lim KW, Goh WHS. Pediatric epilepsy and first afebrile seizure in Singapore: Epidemiology and investigation yield at presentation. *J Child Neurol* 2010;25(10):1216-22.
4. Kwan P, Arzimanoglou A, Berg AT, *et al*. Definition of drug resistant epilepsy: consensus proposal by the ad hoc Task Force of the ILAE Commission on Therapeutic Strategies. *Epilepsia* 2010;51(6):1069-77.
5. Berg AT, Vickrey BG, Testa FM, *et al*. How long does it take for epilepsy to become intractable? A prospective investigation. *Ann Neurol* 2006;60(1):73-9.
6. Engel J, Pedley TA. Epilepsy: A comprehensive textbook, 2nd Edition. Lippincott Williams & Wilkins; 2008.
7. Braun KPJ, Cross JH. Pediatric epilepsy surgery: the earlier the better. *Expert Rev Neurother* 2018;18(4):261-3.
8. Cross JH, Jayakar P, Nordli D, *et al*. Proposed criteria for referral and evaluation of children for epilepsy surgery: recommendations of the Subcommission for Pediatric Epilepsy Surgery. *Epilepsia* 2006;47(6):952-9.
9. Sugano H, Arai H. Epilepsy surgery for pediatric epilepsy: Optimal timing of surgical intervention. *Neurol Med Chir (Tokyo)* 2015;55(5):399-406.
10. Lee KH, Lee YJ, Seo JH, Baumgartner JE, Westerveld M. Epilepsy surgery in children versus adults. *J Korean Neurosurg Soc* 2019;62(3):328-35.
11. Wiebe S, Blume WT, Girvin JP, Eliasziw M, Effectiveness and Efficiency of Surgery for Temporal Lobe Epilepsy Study Group. A randomized, controlled trial of surgery for temporal-lobe epilepsy. *N Engl J Med* 2001;345(5):311-8.
12. Dwivedi R, Ramanujam B, Chandra PS, *et al*. Surgery for drug-resistant epilepsy in Children. *N Engl J Med* 2017;377(17):1639-47.
13. Asadi-Pooya AA, Malekmohamadi Z, Kamgarpour A, *et al*. Corpus callosotomy is a valuable therapeutic option for patients with Lennox–Gastaut syndrome and medically refractory seizures. *Epilepsy Behav* 2013;29(2):285-8.
14. Thuy Le MA, Fong SL, Lim KS, *et al*. Underutilization of epilepsy surgery in ASEAN countries. *Seizure* 2019;69:51-6.
15. Scheffer IE, Berkovic S, Capovilla G, *et al*. ILAE classification of the epilepsies: Position paper of the ILAE Commission for Classification and Terminology. *Epilepsia* 2017;58(4):512-21.
16. Grinnon ST, Miller K, Marler JR, *et al*. National Institute of Neurological Disorders and Stroke Common Data Element Project - approach and methods. *Clin Trials Lond Engl* 2012;9(3):322-9.
17. Blümcke I, Thom M, Aronica E, *et al*. The clinicopathologic spectrum of focal cortical dysplasias: a consensus classification proposed by an ad hoc Task Force of the ILAE Diagnostic Methods Commission. *Epilepsia* 2011;52(1):158-74.
18. Louis DN, Perry A, Reifenberger G, *et al*. The 2016 World Health Organization Classification of Tumors of the Central Nervous System: a summary. *Acta Neuropathol (Berl)* 2016;131(6):803-20.
19. Engel J, ed: Surgical treatment of the epilepsies. 2nd ed. New York: Raven Press; 1993. 786.
20. Dallas J, Englot DJ, Naftel RP. Neurosurgical approaches to pediatric epilepsy: Indications, techniques, and outcomes of common surgical procedures. *Seizure* 2018; 77:76-85.
21. Hader WJ, Tellez-Zenteno J, Metcalfe A, *et al*. Complications of epilepsy surgery-A systematic review of focal surgical resections and invasive EEG monitoring. *Epilepsia* 2013;54(5):840-7.
22. Sacino MF, Ho CY, Murnick J, Keating RF, Gaillard WD, Oluigbo CO. The role of intraoperative MRI in resective epilepsy surgery for peri-eloquent cortex cortical dysplasias and heterotopias in pediatric patients. *Neurosurg Focus* 2016;40(3):E16.
23. Sperling MR. The consequences of uncontrolled epilepsy. *CNS Spectr* 2004;9(2):98-101, 106-9.
24. Boshuisen K, van Schooneveld MMJ, Uiterwaal CSPM, *et al*. Intelligence quotient improves after antiepileptic drug withdrawal following pediatric epilepsy surgery: IQ after AED withdrawal. *Ann Neurol* 2015;78(1):104-14.
25. Eid H, Crevier-Sorbo G, Moreau JT, *et al*. Eight-year experience with 3-T intraoperative MRI integration

in focal pediatric epilepsy surgery: Impact on extent of resection, residual volumes, and seizure outcomes. *Am J Roentgenol* 2020;214(6):1343-51.
26. Edelvik A, Rydenhag B, Olsson I, *et al*. Long-term outcomes of epilepsy surgery in Sweden: a national prospective and longitudinal study. *Neurology* 2013;81(14):1244-51.
27. Englot DJ. A modern epilepsy surgery treatment algorithm: Incorporating traditional and emerging technologies. *Epilepsy Behav* 2018;80:68-74.
28. Englot DJ, Breshears JD, Sun PP, Chang EF, Auguste KI. Seizure outcomes after resective surgery for extra-temporal lobe epilepsy in pediatric patients. *J Neurosurg Pediatr* 2013;12(2):126-33.
29. Bilginer B, Yalnizoglu D, Soylemezoglu F, *et al*. Surgery for epilepsy in children with dysembryoplastic neuroepithelial tumor: clinical spectrum, seizure outcome, neuroradiology, and pathology. *Childs Nerv Syst* 2009;25(4):485-91.
30. Ranger A, Diosy D. Seizures in children with dysembryoplastic neuroepithelial tumors of the brain—A review of surgical outcomes across several studies. *Childs Nerv Syst* 2015;31(6):847-55.
31. Jalilian L, Limbrick DD, Steger-May K, Johnston J, Powers AK, Smyth MD. Complete versus anterior two-thirds corpus callosotomy in children: analysis of outcome. *J Neurosurg Pediatr* 2010;6(3):257-66.
32. Chan AY, Rolston JD, Lee B, Vadera S, Englot DJ. Rates and predictors of seizure outcome after corpus callosotomy for drug-resistant epilepsy: a meta-analysis. *J Neurosurg* 2018;1-10.
33. Shim KW, Lee YM, Kim HD, Lee JS, Choi JU, Kim DS. Changing the paradigm of 1-stage total callosotomy for the treatment of pediatric generalized epilepsy. *J Neurosurg Pediatr* 2008;2(1):29-36.
34. Paolicchi JM, Jayakar P, Dean P, *et al*. Predictors of outcome in pediatric epilepsy surgery. *Neurology* 2000;54(3):642-7.
35. Krsek P, Maton B, Jayakar P, *et al*. Incomplete resection of focal cortical dysplasia is the main predictor of poor postsurgical outcome. *Neurology* 2009;72(3):217-23.
36. Laxer KD, Trinka E, Hirsch LJ, *et al*. The consequences of refractory epilepsy and its treatment. *Epilepsy Behav* 2014;37:59-70.