

## Case Report

# Epilepsy Surgery in Children and Adolescence; Phramongkutklao College of Medicine's Experience

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**Objectives:** To evaluate the safety and efficacy of epilepsy surgery in children and adolescence at Comprehensive Epilepsy Center, Phramongkutklao College of Medicine.

**Material and Method:** Children and adolescents, who underwent epilepsy surgery at Comprehensive Epilepsy Center, Phramongkutklao College of Medicine were identified from the epilepsy surgery database. The following parameters were evaluated: age at surgery, duration of seizure prior to surgery, presurgical work up, presurgical as well as postsurgical neurological/ seizure status and neuropathology (if applicable). All follow-up data were obtained through clinic visits.

**Results:** Fifteen children who underwent epilepsy surgery between January 1, 2003 and March 31, 2005 were identified. Age at surgery ranged from 2.5 years to 19 years (mean age=8.2 years). Seizure duration prior to surgery ranged from 1 year to 17 years (mean=4.7 years). Eight patients (53%) had partial seizures and underwent excisional procedures [5 temporal lobectomy, 2 left frontal corticectomy, and 1 left functional hemispherectomy]. Seven patients (47%) had generalized seizures and underwent anterior 2/3 corpus callosotomy. Pathological information was available for all 8 cases with partial epilepsy. Four out of eight cases with pathological information demonstrated cortical dysplasia, four revealed hippocampal sclerosis, and two patients had dysembryoplastic neuroepithelial tumor (DNET). At follow-up, all 5 patients with temporal lobectomy and a child who underwent functional hemispherectomy were seizure free (follow up period 3-31 months). Two children with extratemporal resective surgery [ left frontal corticectomy ] showed remarkable improvement with rare breakthrough seizures (follow up period= 3 and 19 months respectively). Four out of seven patients with corpus callosotomy had worthwhile improvement of seizures (follow up period=4-19 months), while another two children were seizure free during short-termed follow up postoperatively (follow up period=1 and 2 months). All patients did not have significant neurological deterioration or worsening of seizure after the surgery.

**Conclusion:** Resective epilepsy surgery in Thai pediatric populations in the authors' experience seems to be safe and effective in selected patients. Most children who underwent callosotomy had a significant reduction in intensity and frequency of tonic, atonic, and tonic-clonic seizures. Dual pathology was common in refractory temporal lobe epilepsy with hippocampal sclerosis. Although the study sample was small, it did advocate several larger studies with the same findings.

**Keywords:** Epilepsy surgery, Pediatrics, Adolescence, Corpus callosotomy

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Burden of epilepsy to the child's life is tremendous. Risks of recurrent seizures include cognitive impairment, physical injury, unexplained death<sup>(1)</sup>, progressive changes in cerebral structure or function, and psychosocial problems. Uncontrolled chronic epilepsy has the potential for irreversible cognitive, behavioral, and psychosocial problems in later life and functional recovery is greatest when seizures are controlled early (plasticity).

When sequential monotherapy or combination of antiepileptic medications fail to control seizures, the likelihood that seizures will be cured with further drug regimen is very unlikely. Kwan and Brodie<sup>(2)</sup> followed 525 patients with new onset epilepsy with a median follow-up period of 5 years. Epilepsy was controlled by the first drug in 47% of the patients and only 11% of patients who did not respond to the first drug due to lack of efficacy responded to a second drug. With a third drug monotherapy or polytherapy, only 1% and 3% responded to the treatment, respectively. This important information warrants the need to consider alternative treatment early in patients; especially in children, who did not respond to adequate treatment with one or two antiepileptic drugs.

The advent of long-term Video-EEG, conventional MRI, functional MRI, SPECT (single photon emission computerized tomography), PET scan (positron emission tomography)<sup>(3)</sup>, and cortical mapping allow us to accurately localize seizure foci and eloquent cortex; thus, precise excision of the cerebral area that creates seizure activities can be made without threatening important cortical areas. For this reason, the neurological function of the child can be safely preserved after the surgery.

Epilepsy surgery for children with refractory epilepsy has been introduced and has become a standard alternative treatment for intractable childhood epilepsy<sup>(4-6)</sup> and can be performed safely and effectively in children at any age from infancy through early childhood and adolescence. A number of surgical procedures have been developed, which include resective surgery (temporal lobectomy, extratemporal resection, hemispherectomy) and palliative surgery (corpus callosotomy and multiple subpial transection).

Phramongkutklao Comprehensive Epilepsy Center was established in 2003 to provide comprehensive treatment medically and surgically for both children and adults who suffer from epilepsy. The objective of the present study was to address the safety and efficacy of epilepsy surgery in Thai children with intractable epilepsy performed at the authors' center.

## Material and Method

The present study comprised 15 children and adolescents (age less than 20 years) with refractory localization-related epilepsy or symptomatic generalized epilepsy who underwent epilepsy surgery at the authors' comprehensive epilepsy center between January 2003 and March 2005. All surgical candidates had localization-related partial epilepsy or symptomatic generalized epilepsy with frequent seizures refractory to multiple antiepileptic drugs. Seizure type was classified by the criteria proposed by the Commission on Classification and Terminology of the International League Against Epilepsy (ILAE).

In all children, electroencephalography (EEG), including conventional EEG and prolonged video-EEG monitoring with 10-20 scalp electrodes, was carried out in the epilepsy monitoring unit before surgery. Video-EEG investigation was performed with Stellate software for automatic spike

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detection recording at least 3 days to capture an appropriate amount of data. Ictal events and interictal spikes were analysed on the basis of localization and lateralization. Magnetic resonance images (MRI) were obtained for all patients on a 1.5 Tesla Signa unit. Sagittal T1-weighted images, T2-weighted as well as FLAIR sequence axial and coronal images were obtained, using a 5-mm slice thickness. Supplemented investigations were performed in some patients if clinically indicated (ictal single-photon emission tomography, WADA evaluation, and neuropsychiatric evaluation). Neuroimaging studies, EEG, and all clinical data on each patient were reviewed at Phramongkutklo's epilepsy conference before decisions about surgical candidacy. All patients underwent craniotomy under general anesthesia.

All resected tissues were taken en bloc, which enabled a thorough pathologic examination. Tissue was processed for conventional histology and immunohistochemistry. The database was queried for age at surgery, duration of seizure prior to surgery, presurgical work up, presurgical as well as postsurgical neurological/ seizure status and neuropathology (if applicable). Outcome is evaluated with a modified Engel classifications as follows: Class I, the patient was seizure-free or had only non-disabling simple partial seizures; Class II, greater than 90% reduction of seizure frequency but the patient continued to experience rare complex partial seizures; Class III, 50-90% reduction in seizure frequency; and Class IV, less than 50% reduction in seizure frequency. All follow-up data were obtained through clinic visits.

## Results

The authors identified 15 children with refractory epilepsy who underwent epilepsy surgery between January 2003 and March 2005 and could be contacted. Age at surgery ranged from 2.5 years to 19 years (mean age=8.2 years). Seizure duration

prior to surgery ranged from 1 year to 17 years (mean=4.7 years) and age at seizure onset ranged from birth to 12 years (mean = 3.7 years). Presurgical evaluation with routine EEG, long-term video-EEG monitoring, and brain MRI were performed in all patients. Two patients with temporal lobe epilepsy underwent WADA evaluation. All five patients with temporal lobe epilepsy had presurgical neuropsychiatric evaluation. SPECT (single photon emission computerized tomography) was performed in a child with extratemporal epilepsy arising from the left premotor area. Eight patients (53%) had partial seizures and underwent excisional procedures (5 temporal lobectomy, 2 left frontal corticectomy, and 1 left functional hemispherectomy). Intraoperative cortical stimulation to identify eloquent motor area was performed in both patients who underwent frontal corticectomy. Seven patients had generalized seizures and underwent anterior 2/3 corpus callosotomy.

Pathological information was available for all 8 cases with partial epilepsy. Four out of eight cases with pathological information demonstrated cortical dysplasia (temporal lobectomy=2, hemispherectomy=1, and left frontal corticectomy=1). Four out of five patients with temporal lobe epilepsy had hippocampal sclerosis, two children (temporal lobe epilepsy=1, extratemporal epilepsy=1) had dysembryoplastic neuroepithelial tumor (DNET), and two out of four patients with temporal lobe epilepsy from hippocampal sclerosis had additional pathology with cortical dysplasia at temporal neocortex.

At follow-up, all 5 children with temporal lobectomy were seizure free (Engel Class I, follow up period = 3-31 months). There was no deterioration in their cognitive functions as well as their baseline neurological functions except for asymptomatic visual field defect.

A young boy who underwent left functional hemispherectomy became seizure free (Engel class

**Table 1.** Patient's baseline seizure character, surgical treatment, and outcome

Patient	Procedure	Diagnosis	Age at surgery	Age at seizure onset	AED	Seizure types	Baseline seizures	Postsurgery seizures	pathology	F/U period
1	Ant.2/3 Corpus collosotomy	LGS	6 years	1 year	LTG, VPA	Tonic Sz	5/day	1-2/day	N/A	16 months
2	Ant.2/3 Corpus collosotomy	LGS	4 years	2 years	TPX, VPA	Tonic Sz	2-3/day	0-1/day	N/A	19 months
3	Ant.2/3 Corpus collosotomy	LGS	7 years	1 month	VPA, CLZ, PB, PHT	Tonic Sz	3-4/day	1-2/day	N/A	10 months
4	Ant.2/3 Corpus collosotomy	LGS	2.5 years	3 months	VPA, LEV, CLB	Myoclonic Absence	3-4/day	Unchanged	N/A	13 months
5	Ant.2/3 Corpus collosotomy	LGS	4 years	2 months	LTG, CLB	Tonic	8-9/day	Unchanged	N/A	2 months
6	Ant.2/3 Corpus collosotomy	LGS	5 years	3 months	LEV, CLZ, OXC, VPA	Myoclonic Tonic	5-6/day	None	N/A	4 months
7	Ant.2/3 Corpus collosotomy	3.5 years	birth		VPA	Tonic	2-3/day	None	N/A	1 month
8	Right temporal lobectomy	MTLE	9 years		TPX, VPA	Myoclonic	3-4/day	None	N/A	10 months
9	Left temporal lobectomy	MTLE	13 years	7 years	VPA, TPX, OXC	Tonic	2-3/day	None	MTS	27 months
10	Right temporal lobectomy	MTLE	13 years	12 years	CBZ, VPA	CPS	3-4/month	none	MTS CD	31 months
11	Left temporal lobectomy	MTLE	6 years	15 months	CBZ, VPA, TPX	CPS	1-2/month	none	MTS CD	14 months
12	Left temporal lobectomy	MTLE	19 years	2 years	PHT, VPA	CPS	2-3/month	none	MTS	3 months
13	Left functional hemispherectomy	Hemicortical dysplasia	3 years	5 months	VPA, TPX, CLZ	Tonic right side spasm	3-4/day	none	CD	10 months
14	Left frontal corticectomy	Focal cortical	11 years	10 years	OXC, VPA, CLZ	Tonic right side spasm	5-10/day	rare seizure with illness	CD	19 months
15	Left frontal corticectomy	DNET	13 years		VPA, CBZ	Tonic posturing of right arm, clonic twitching of right face	2-3/month	rare seizure	DNET	3 months

**Abbreviation:** MTS= Mesial temporal sclerosis, MTLE= Mesial temporal lobe epilepsy, DNET= Dyssembryoplastic neuroepithelial tumor, CD= Cortical dysplasia GTC= Generalized tonic-clonic convulsion, CPS, Complex partial seizures, LTG= Lamotrigine, VPA=Valproate, TPX= Topiramate, CLZ= Clonazepam, PB= Phenytoin, LEV= Levetiracetam, CLB= Clobazam, OXC= Oxcarbazepine, CBZ= Carbamazepine N/A= Not applicable

I, follow up period = 10 months). There was no worsening of his preexisting non-functional right hemiparesis or any development of new neurological deficit. In fact, his right arm became more mobilized and he was more alert and socialized when compared to the pre-surgical period.

Two patients with extratemporal resective surgery after intraoperative cortical stimulation to identify functional motor area (frontal corticectomy) showed remarkable improvement with rare breakthrough seizures (Engel Class II, follow up period = 3 and 19 months respectively). Although, their epileptogenic lesions lay very approximate to the eloquent motor area, both boys did not suffer any new neurological deficit, particularly hemiparesis after the surgery.

Four out of seven patients with corpus callosotomy had worthwhile improvement (more than 50% reduction of severity or frequency of at least one seizure type (Engel Class III, follow up period = 1-19 months) and another two children were seizure free, although the follow up period was quite short (one and two months respectively). There was no postoperative complication for all of these patients.

## Discussion

A recent study has indicated that if a patient has not responded to 2 antiepileptic drugs, the likelihood of becoming seizure free with additional medications is minimal (less than 5%)<sup>(1)</sup>. Since repeated seizures may result in neuronal damage, lost school days, and the morbidities that occur with antiepileptic drugs; alternative treatment such as epilepsy surgery or vagus nerve stimulation should be considered earlier than later when medical treatment fails to result in seizure control. Surgical treatment of intractable seizures in children has now become part of the standard therapies and can be performed at any age in the pediatric population from infancy through early childhood and adolescence.

This series described Phramongkutklao Comprehensive Epilepsy program's experience with epilepsy surgery in childhood and adolescence. To the authors' knowledge, this is the first study to describe efficacy, safety, and surgical outcome of various types of epilepsy surgery including temporal lobectomy, extratemporal surgery, hemispherectomy, and corpus callosotomy in Thai children. The present series support other studies' finding that temporal lobectomy was an effective treatment of seizures arising in the mesial structures or lateral temporal neocortex and excellent outcomes were achieved in at least 70-80% of children<sup>(7-11)</sup> as all of the presented five patients who underwent temporal lobectomy; regardless of the side of surgery or surgical pathology, became seizure free without new neurological deficits other than asymptomatic visual field defects.

The outcome rate of surgery for intractable extratemporal epilepsy in two of the presented patients with left frontal corticectomy resulted in a lower rate of seizure freedom (Engel class II) compared to temporal lobectomy (Engel class I)<sup>(4-6,8)</sup> which was also in congruence with other series<sup>(4-6,8)</sup>, that reported a lower rate of seizure freedom than temporal lobe epilepsy with the ranges from approximately 20% to 80%. However, quality of life of both patients improved remarkably as they experienced only rare seizures with intercurrent illness when compared to presurgical seizure frequency of several times daily in one child and several times monthly in the other. Furthermore, both child did not suffer any neurological deficits after the surgery despite the fact that the epileptogenic lesions were adjacent to the motor area.

After the first report of hemispherectomy for the treatment of intractable epilepsy in 1938 by McKenzie<sup>(12)</sup>, dramatic improvement in children with intractable epilepsy associated with unilateral hemispherical pathology resulted in further use of

this procedure in epilepsy centers. Hemispherectomy provides seizure relief in 60% to 80% of patients with hemispherical pathologies such as Sturge-Weber, hemimegaencephaly or Rasmussen syndromes<sup>(13-15)</sup>. The surgical outcome of a presented young child (patient#13) with left hemicortical dysplasia who underwent left functional hemispherectomy and became seizure-free also advocated the effectiveness of this type of surgery and also clearly demonstrated that the surgery can be performed safely in a very young children even with extensive cortical resection. Indeed, his right hemiparesis became visibly improved as well as his alertness and socialization postsurgically. This suggests that brainstorm with repetitive epileptiform activities may interrupt the normal function of neighboring healthy brain and early effective treatment to provide complete seizure control will certainly enhance the developmental potential of the child in all aspects.

Although corpus callosotomy is only effective as a palliative but not a cure for treatment of atonic, tonic-clonic and tonic seizures in which no single focus can be identified, many of the presented patients experienced significant seizure relief in at least one seizure type (Engel class II) which resulted in a better quality of life for both the patients and their caregivers. Since the follow up period for some of these patients was not long enough, it would be too premature to make a conclusion regarding the effectiveness of this procedure. No patients in the presented series experienced any potential morbidities which included more intense seizures and new aphasia when compared to their presurgical neurological status.

Most common pathology found in the present series was cortical dysplasia. This finding was similar to other studies that found cortical dysplasia were present in 68% of infants and in 26% of children and adolescents with medically refractory epilepsy in recent surgical series. Other

common pathologies included hippocampal sclerosis and dysembryoplastic neuroepithelial tumor, which also have been well documented to be commonly associated with intractable partial epilepsy in children. Interestingly, dual pathology was common in the present series as two out of four patients with temporal lobe epilepsy from hippocampal sclerosis also had cortical dysplasia at temporal neocortex. There was no difference in clinical semiology, clinical history or surgical outcome between children with or without dual pathology who underwent temporal lobectomy in the present study. This finding supported other studies<sup>(16-22)</sup> that found dual pathology quite common. In one series, approximately 25% of patients with severe hippocampal sclerosis had developmental abnormalities on histopathology. Furthermore, no consistent differences in clinical history or seizure semiology between patients with cortical dysplasia and those with pure hippocampal sclerosis have been reported. In another pediatric surgical series including 34 children and adolescents with HS, many with findings suggesting cortical dysplasia in the ipsilateral temporal neocortex, the presence of dual pathology did not portend a poor prognosis because 90% of the subjects were seizure free after temporal resection.

## Conclusion

The present series further supports cortical resection as a definitive treatment for intractable partial epilepsy in pediatric and adolescence. This treatment seems to be safe and effective in selected pediatric patients with intractable epilepsy. The authors believe that remission of a debilitating disorder during a period of rapid brain and psychosocial maturation will be greatly beneficial to these unfortunate children to meet their potential developmental aspects. Although the follow up period for children who underwent corpus callosotomy was quite short to make a definite

conclusion, many of these children had significant reduction in intensity and frequency of tonic, atonic, and tonic-clonic seizure and improve the quality of life of both patients and care givers.

Cortical dysplasia and hippocampal sclerosis were the most common pathologies found in children with refractory epilepsy who underwent resective surgery and dual pathology was common in refractory temporal lobe epilepsy with hippocampal sclerosis in the present study. Although the presented population was small, it did advocate several larger studies with similar findings.

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## การรักษาโรคลมชักโดยการผ่าตัดในผู้ป่วยเด็กและวัยรุ่น: ประสบการณ์ของศูนย์โรคลมชักครบวงจร โรงพยาบาลพระมงกุฎเกล้า

ชาครินทร์ ณ บางช้าง, สิริจันต์ สกุลณมรรคา, ไพสิฐ เพือกสกนธ์, โยธิน ชินวลัญช์

**วัตถุประสงค์:** เพื่อศึกษาประสิทธิภาพและความปลอดภัยของการรักษาโรคลมชัก โดยการผ่าตัดในผู้ป่วยเด็กและวัยรุ่น ณ ศูนย์โรคลมชักครบวงจร โรงพยาบาลพระมงกุฎเกล้า

**วัสดุและวิธีการ:** เป็นการวิเคราะห์ข้อมูลย้อนหลัง ในผู้ป่วยเด็กและวัยรุ่น ที่มีการชักชนิดรุนแรง และเข้ารับการรักษาโดยการผ่าตัด ณ โรงพยาบาลพระมงกุฎเกล้า โดยศึกษาข้อมูลดังต่อไปนี้ คือ อายุในขณะที่ได้รับการผ่าตัด, ระยะเวลาของการชักก่อนเข้ารับการผ่าตัด, ภาวะการทำงานทางระบบประสาท และความรุนแรงของการชักก่อนและหลังการผ่าตัด, ข้อมูลการตรวจเพื่อคัดเลือกผู้ป่วยและวางแผนการผ่าตัดก่อนเข้ารับการผ่าตัด, และผลการตรวจทางชิ้นเนื้อ

**ผลการศึกษา:** มีเด็กและวัยรุ่นอายุระหว่าง 2.5 - 19 ปี จำนวน 15 ราย เข้ารับการรักษาโรคลมชักโดยการผ่าตัดระหว่าง วันที่ 1 มกราคม พ.ศ. 2546 ถึง วันที่ 31 มีนาคม พ.ศ. 2548 โดยมีระยะเวลาของการชักก่อนการผ่าตัดระหว่าง 1 - 17 ปี (เฉลี่ย 4.7 ปี) มีผู้ป่วย 8 ราย (ร้อยละ 53) เข้ารับการผ่าตัดสมองบางส่วน (ผ่าตัดสมองส่วน Temporal ในผู้ป่วย 5 ราย, ผ่าตัดสมองส่วน Frontal ในผู้ป่วย 2 ราย) และผ่าตัดสมองทั้งซีก (Hemispherectomy ในผู้ป่วย 1 ราย) และผู้ป่วย 7 ราย (ร้อยละ 43) เข้ารับการรักษาโดยการผ่าตัดสมองส่วน corpus callosum หลังการผ่าตัด ผู้ป่วยทุกรายที่รับการผ่าตัดสมองส่วน Temporal และผู้ป่วยที่รับการผ่าตัดสมองทั้งซีก ไม่มีอาการชักอีก (ระยะเวลาการติดตาม 3 - 31 เดือน) ผู้ป่วยที่รับการผ่าตัดสมองส่วน Frontal มีอาการชักลดลงอย่างชัดเจน (ระยะเวลาการติดตาม 3 และ 19 เดือน) ส่วนผู้ป่วยที่รับการรักษา โดยการผ่าตัดสมองส่วน corpus callosum มีอาการชักลดลงอย่างมีนัยสำคัญ (ระยะเวลาการติดตาม 4 - 19 เดือน) ผู้ป่วยทุกรายไม่มีผลแทรกซ้อน จากการผ่าตัด ไม่มีปัญหาทางระบบประสาทที่เพิ่มขึ้น และไม่มีการชักที่รุนแรงเพิ่มขึ้น

**สรุป:** การรักษาโรคลมชักโดยการผ่าตัดในผู้ป่วยเด็กและวัยรุ่นในประสบการณ์ ของคณะผู้รักษามีประสิทธิภาพและความปลอดภัยสูง และช่วยเพิ่มคุณภาพชีวิตของทั้งผู้ป่วย และผู้ดูแลเป็นอย่างมาก ซึ่งผลการรักษาดังกล่าวสอดคล้องกับข้อมูล ส่วนใหญ่ในต่างประเทศที่มีผู้ป่วยในการศึกษาจำนวนมาก และมีผลสรุปเช่นเดียวกัน

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