



Underutilization of epilepsy surgery in ASEAN countries

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ABSTRACT

Purpose: This survey was performed to determine the availability of epilepsy surgery, and understand the limiting factors to epilepsy surgery in ASEAN countries with total of 640 million population.

Method: A cross-sectional survey was completed by national representatives in all ASEAN countries (Brunei, Cambodia, East Timor, Indonesia, Laos, Malaysia, Myanmar, Philippines, Singapore, Thailand, and Vietnam).

Results: Overall facilities for initial epilepsy pre-surgical evaluation are available in most countries, but further non-invasive and invasive investigations are limited. Three countries (Brunei, Cambodia, and East Timor) have no epilepsy center, and 2 countries (Laos, Myanmar) have level 2 centers doing tumor surgery only. Level-3 epilepsy centers are available in 6 countries (Indonesia, Malaysia, Philippine, Singapore, Thailand, Vietnam); only 5 countries (Indonesia, Malaysia, Philippine, Singapore, Thailand) has at least one level-4 epilepsy care facility. Indonesia with 261 million population only has one level 3 and another level 4 center. The costs of presurgical evaluation and brain surgery vary within and among the countries. The main barriers towards epilepsy surgery in ASEAN include lack of expertise, funding and facilities.

Conclusions: Epilepsy surgery is underutilized in ASEAN with low number of level 3 centers, and limited availability of advanced presurgical evaluation. Lack of expertise, facilities and funding may be the key factors contributing to the underutilization.

1. Introduction

Approximately 70 million people currently live with epilepsy worldwide [1]. The availability and accessibility of antiepileptic drugs has been an issue for developing countries. In Asia, the treatment gap has ranged from 28% to as high as 98% [2]. For those who received antiepileptic drugs, there were about one-third of patients who still

continue to have seizures [3]. Patients with drug-resistant epilepsy are potential candidates for surgery especially those with surgically remediable syndrome, such as mesial temporal sclerosis or focal cortical dysplasia. A systematic review reported a good surgical outcome in 50–67% of those with epilepsy surgery with seizure free duration up to 5 years [4]. Majority (80%) of the patients with epilepsy surgery reported better overall quality of life comparing to before surgery [5]. For

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children with intractable epilepsy, epilepsy surgery led not only better quality of life but also improvement in cognitive development [6]. Therefore, patients who meet criteria for drug-resistant epilepsy should be evaluated early for surgical treatment.

Epilepsy surgery gap is defined by the percentage of patients who are eligible for surgery but did not receive surgery [7]. In United States (USA), epilepsy surgery gap was reported to be as high as 96–99% [7]. A study in Canada reported that only 2.2% of patients were referred for epilepsy surgery within 2 years of being defined as medically refractory [8]. In one epilepsy center in United Kingdom, up to 66.6% of patients with refractory focal epilepsy did not proceed to surgery [9]. In India, only 200 epilepsy surgeries (0.04%) were performed per year despite having over 500,000 potential epilepsy surgery candidates [10]. These data showed that epilepsy surgery is underutilized worldwide.

Barriers to epilepsy surgery are multifactorial, including clinical, physician-, patient- and healthcare-system-related factors. The clinical factors include diagnostic difficulties in defining the epileptogenic zone or unacceptable surgical risks, e.g. epileptogenic zone within the eloquent cortex [9,11]. Physician-associated barriers include low referral rate due to lack of knowledge on drug-resistant epilepsy or misconceptions regarding brain surgery [8,9,12], and lack of expertise, especially in low income and developing countries [13]. In addition, 21–24% of potential surgical candidates refused epilepsy surgery due to fear of surgery and its complications, and seizure tolerance [9,11]. In low-income countries, lack of facilities and funding are major barriers for epilepsy surgery.

In a review, Wieser et al. reported at least 26 out of 142 (18.3%) economically disadvantaged nations have at least 1 epilepsy center, compared with 18 out of 24 (75%) developed countries, using a search in Medline and proceeding from International Epilepsy Congress from 1991 to 1999 [14]. However, to the best of our knowledge, there is no study surveying on the accessibility of epilepsy surgery services in this part of the world. The Association of Southeast Asian Nations (ASEAN) consists of 11 countries with a total of 640 million population. There are 6 countries with large population of more than 50 million, namely Indonesia (260 millions), Philippines (105), Vietnam (92), Thailand (69) and Myanmar (55). The others are Malaysia (31), Cambodia (16), Laos (6.8), Singapore (5.6), East Timor (1.3) and Brunei (0.4). Of these 11 countries, only two (Brunei and Singapore) are labelled as economically developed, accounting for 1% of total population; whereas the remaining population are of middle or low-income category. This survey aimed to understand the availability of epilepsy surgery in ASEAN and to identify the perceived limiting factors to epilepsy surgery in each country.

2. Methods

We conducted a cross-sectional survey by sending electronic mails to respective national representatives in all ASEAN countries, including Brunei, Cambodia, Indonesia, Laos, Malaysia, Myanmar, Philippines, Singapore, Thailand and Vietnam, except East Timor. Information on East Timor was obtained via personal communication. This survey was performed as a collaboration under the ILAE Commission of Asian-Oceanian Affairs (CAOA) Research Task Force and completed in May 2018.

2.1. Questionnaires

The questionnaires focused on two main areas: (1) determining the availability of epilepsy surgery, and (2) understanding the limiting factors to epilepsy surgery in each ASEAN country.

For (1), the collaborators were asked about (a) the number of epilepsy centers, and the names of the centers, (b) the number of personnel involved in epilepsy surgery including neurologists, neurosurgeons and paediatric neurologists, (c) the available epilepsy pre-surgical evaluation facilities and the number of centers performing these services, (d)

the types of surgery provided in each center, including curative and palliative surgery, and (e) cost estimation for brain surgery and the pre-surgical evaluation procedures such as MRI brain, routine EEG and VEEG.

For (2) a general question was asked on the major factor(s) limiting epilepsy surgery.

2.2. Operational definition

A Magnetic Resonance Imaging (MRI) epilepsy protocol was defined as one which includes a T1 volumetric study (e.g. MRPAGE or FSPGR), and an oblique coronal plane perpendicular to the hippocampus axis. Routine Electroencephalograph (EEG) was defined as video-EEG recording for at least 30 min, with activation procedures e.g. photic stimulation and hyperventilation. A center is considered to perform sleep EEG recordings if sleep is recorded in 50% of all routine EEGs. A center is considered to provide long-term video-EEG monitoring (VEM) if the recording of video-EEG is 24 h or more. According to the Guidelines for the services, personnel and facilities at specialized Epilepsy centers, epilepsy centers are identified based on four level of epilepsy care [15]. An evaluation in emergency room or primary care physician's office is considered level one. Level 2 care is with neurologist and initial evaluation including video-EEG. Level-3 center is a center which offers noninvasive evaluation for epilepsy surgery including long-term video-EEG monitoring and straightforward lesionectomy including brain tumor and non-brain tumor (mesial temporal sclerosis, focal cortical dysplasia). Level-4 epilepsy center provides more complex evaluation such as intracranial electrodes and broad range of surgical procedures including corpus callosotomy, hemispherectomy and resection of MRI-negative cases.

Population and classification by income were according to World Bank's data 2016 [16]. The Gross Domestic Product (GDP) per capita used in this study was taken from the International Monetary Fund report from October 2017 [17].

3. Results

3.1. Epilepsy centers and personnel

There is at least one epilepsy center in each ASEAN country (range from 1 to 9 centers per country) except Brunei, Cambodia and East Timor. In Brunei and Cambodia, there was no neurosurgeon or paediatric neurologist involved in epilepsy surgery, thus only initial epilepsy presurgical evaluation is provided but not epilepsy surgery. In East Timor, there is one neurologist, but no MRI brain, EEG or epilepsy surgery services. Six countries have less than one center per 10 million population. The population per neurologist involved in epilepsy surgery ranges from 0.13–25.83 million people, except East Timor. There was a total of 62 neurologists who have undergone 6-month epilepsy/EEG fellowship in ASEAN, but none from Brunei, East Timor, Laos and Myanmar [18] (Table 1).

3.2. Epilepsy pre-surgical evaluation

a) Non-invasive evaluation:

In ASEAN, Laos and Myanmar have only level 2 epilepsy centers, level-3 centers are available in 6 countries (54.5%) and only five countries (45.5%) provide level-4 cares. Facilities for initial epilepsy pre-surgical evaluation (routine and sleep EEG, and MRI brain) are available in most countries. Video-EEG telemetry is available in 54.5% of the countries. Further non-invasive neuroimaging such as single-photon emission computed tomography (SPECT) and/or positron-emission tomography (PET) scans can be performed in 45.5% of the SEA countries. Other specific investigations such as EEG source imaging (ESI), magnetoencephalography (MEG) and morphometric analysis are only available in certain countries such as

Table 1
Number of epilepsy centers and clinicians involved in epilepsy surgery in each country.

Country	No of epilepsy center	Neurologist	Neurosurgeon	Paediatric neurologist	Population (million)	Population per neurologist (million)	No. of centers per pop. (10 million)	No. of neurologist undergone epilepsy/EEG fellowship
Brunei	0	3	0	0	0.4	0.13	0	0
Cambodia	0	11	20	0	16.0	1.45	0	2
East Timor	0	0	0	0	1.26	1.26	0	0
Indonesia	5	15	15	10	261.1	17.41	0.2	10
Laos	1	3	3	1	6.8	2.27	1.5	0
Malaysia	4	7	10	6	31.2	0.22	1.3	10
Myanmar	8	25	18	7	52.9	2.12	1.5	0
Philippines	4	4	1	4	103.3	25.83	0.4	10
Singapore	4	4	2	2	5.6	1.4	7.1	10
Thailand	7	15	7	15	68.9	4.59	1.0	10
Vietnam	9	20	30	5	92.7	4.64	0.9	10
Total	42	107	106	50	640.2	6.00	0.66	62

Table 2
Number of epilepsy centers in ASEAN with non-invasive and invasive epilepsy pre-surgical evaluation.

Country	No of level 2/3 center	No of level 4 center	Total no of epilepsy center	Non-invasive							Invasive	
				Routine EEG	Sleep EEG	MRI brain	VEEG	Ictal SPECT	PET	Others	Depth/subdural electrode implantation	SEEG
Brunei	0	0	0	2	0	2	0	0	0	0	0	0
Cambodia	0	0	0	1	0	1	0	0	0	0	0	0
East Timor	0	0	0	0	0	0	0	0	0	0	0	0
Indonesia	3/1	1	5	5	5	4	2	0	1	1	1	0
Laos	1/0	0	1	1	0	0	0	0	0	0	0	0
Malaysia	2	2	4	4	4	4	4	1	2	MEG, ESI, Morphometric analysis	2	0
Myanmar	8/0	0	8	8	8	8	0	0	0	0	0	0
Philippines	2	2	4	4	4	4	4	1	2	0	2	0
Singapore	2	2	4	3	3	3	3	0	2	Morphometric analysis	2	0
Thailand	2	5	7	7	6	7	7	6	5	Morphometric analysis	5	1
Vietnam	5/4	0	9	9	5	9	4	0	0	0	0	0

MEG, Magneto-encephalography; ESI, EEG source imaging; SEEG, stereo-encephalography.

Malaysia, Singapore and Thailand (Table 2).

b) Invasive evaluation:

Invasive epilepsy presurgical evaluation such as depth or subdural electrode implantation is available in 5 out of 11 (45.5%) countries. Thailand is the only country in the region performing stereo-encephalography (SEEG) (Table 2).

3.3 Epilepsy surgery

a) Types of epilepsy surgery:

All but 3 countries (Brunei, Cambodia and East Timor) in the region have various types of epilepsy surgeries done (72.7%). The most commonly performed epilepsy surgery is lesionectomy for brain tumor, followed by lesionectomy for non-brain tumor such as mesial temporal sclerosis and focal cortical dysplasia. Resective surgery for MRI-lesion negative cases is performed in five countries, and palliative surgery such as callosotomy, vagal nerve stimulation, hemispherectomy or hemispherotomy in six countries (Table 3).

b) Cost of epilepsy surgery (USD):

Table 4 shows the cost estimation for epilepsy surgery in ASEAN region. The costs of initial evaluation such as EEG or MRI vary within and among the countries. The variation in cost estimation within a country is due to the presence of different healthcare system such as public and private healthcare systems. Routine EEG costs below 100 USD in most countries, whereas the price of MRI ranges from 0 to 1000 USD. The greatest variation of cost estimation is seen in brain surgery, varies between 0–60,000 USD. The overall cost of epilepsy surgery from pre-surgical evaluation to the brain surgery can be as low as less than 100 USD in countries such as Malaysia, Myanmar, Philippines and Laos, but more than 10,000 USD in Philippines and Singapore.

3.4. Limiting factors

The main barriers towards epilepsy surgery in ASEAN include lack of funding, facilities and expertise, and lack of interest or referral among the clinicians (Table 5).

4. Discussion

Epilepsy surgery has been performed in ASEAN since the end of '90s but its availability lags significantly behind that in several other regions in the world [19–21]. There are totally 41 epilepsy centers serving 640 million population in ASEAN, less than one center for 10 million population. This number is low when compared to other Asian countries with more than one center serving 10 million population, such as Korea (14 centers for 48 million population) [22], Taiwan (3 centers for 23 million) [23] or Hong Kong (3 centers for 7 million) [24]. In addition to limited availability, there are only a small number of clinicians involved in epilepsy surgery. An estimation of 200–300 cases of epilepsy surgery was performed per year in ASEAN countries, based on personal communication, markedly lower than Korea or Japan, which are doing a similar number of epilepsy surgeries every year despite a smaller population (Japan 127 million and Korea 51 million versus ASEAN 640 million) [22,25]. Epilepsy surgery is still underutilized in this region and advanced techniques are not widely available. There are numerous possible factors which potentially combine to prevent establishment and sustainment of epilepsy surgery programs. These may vary from country to country and be true to varying degrees within a country.

Table 3
Types of epilepsy surgery and number of centres performing these surgeries in each country.

Country	Lesionectomy (brain tumor)	Lesionectomy (non-brain tumor) [*]	Resection for MRI- negative cases	Callosotomy	VNS	Hemispherectomy/ Hemispherotomy
Brunei	0	0	0	0	0	0
Cambodia	0	0	0	0	0	0
East Timor	0	0	0	0	0	0
Indonesia	5	3	1	2	2	2
Laos	1	0	0	0	0	0
Malaysia	4	4	2	3	4	2
Myanmar	7	0	0	0	0	0
Philippines	4	2	2	2	0	2
Singapore	4	3	2	1	2	1
Thailand	7	5	5	7	5	5
Vietnam	9	6	0	1	0	1

* Non-tumor conditions include mesial temporal sclerosis (MTS) and focal cortical dysplasia (FCD); VNS, vagal nerve stimulation.

4.1. Expertise

Lack of expertise is one of the main barriers towards epilepsy surgery. To successfully establish an epilepsy center, a team with various expertise including epileptologists or neurologists subspecialized in epilepsy, neurosurgeons interested or experienced in epilepsy surgery, EEG technologists trained in an epilepsy center. Thus, in resource-limited countries, epilepsy surgery requiring a multidisciplinary team poses challenges. According to ILAE Neurosurgery Commission report in 2000, a basic epilepsy center has a catchment of 2 million population and a reference epilepsy center has a population basis of 4–10 million [26]. Comparing to this report, most ASEAN countries have less than 1 center per 10 million population, of which only a few can provide level-4 epilepsy care. Of the epilepsy surgery centers listed in ASEAN countries, only 3 out of 5 in Indonesia and 2 out of 4 in Philippines perform lesionectomy for non-tumor conditions such as MTS and FCD. The others can only perform lesionectomy for brain tumor, because there is no long-term video EEG monitoring, which limits the range of surgery. This limitation can be explained by lack of subspecialty training in epilepsy.

The column of “Neurologists” in Table 1 represented the number of neurologists who are involved in epilepsy surgery including performing presurgical evaluation. However, the level of sub-specialization of neurologists in each country varied. In ASEAN, all countries except Singapore has less than 1 neurologist per 100,000 population [27]. In addition, most neurologists in ASEAN countries practice general neurology and this has resulted in a lack of epilepsy sub-specialization and consequent lack of epilepsy surgery services in the region [27]. Brunei and Cambodia are unable to perform epilepsy surgery because there is no neurosurgeon involved in epilepsy management.

An estimated half of the cases with refractory focal epilepsy are non-lesional on MRI, but only half of the ASEAN countries perform invasive monitoring and surgery in MRI-negative cases. Only 62 neurologists

Table 4
Cost estimation for epilepsy presurgical evaluation and surgery in each country, in US dollars (USD), in comparison with the GDP per capita.

Country	GDP per capita, USD (2017)	Brain surgery	MRI	EEG	Video telemetry	Estimated total amount
Brunei	27,893		600-900	50		
Cambodia	1,389		140	50		
East Timor	2,208					
Indonesia	3,858	7,000-10,000	250-300	40-100	120	7,640-10,740
Laos	2,567	600-1000	200-300	42-45		840-1,345
Malaysia [*]	9,659	100-250-2550-10,000	200-300-400	12-15-50-100	20-30-100	370-10,800
Myanmar	1,272	0-2,000	70-150	10-20		80-2,170
Philippines	3,022	0-16,000	0-300	20-60	400-500	1,220-17,860
Singapore	53,880	20,000-60,000	800-1000	100-200	400-800	22,100-63,600
Thailand	6,336	2,000 – 4,500	400 – 475	80 – 100	350 – 500	3,500 – 6,500
Vietnam	2,306	2,000	150 – 200	10-20	100 – 200	2,600

* Cost variation in different healthcare systems (including public, university and private hospitals).

Table 5
Limiting factors for epilepsy surgery in ASEAN.

Country	Funding	Facilities	Expertise	Clinician [*]	Patient
Brunei		Y	Y		Small population
Cambodia	Y	Y	Y	Y	
East Timor					
Indonesia	Y	Y			
Laos	Y	Y	Y		
Malaysia	Y	Y			Fear
Myanmar	Y	Y	Y		
Philippines	Y			Y	
Singapore	Y	Y		Y	
Thailand	Y	Y	Y		
Vietnam	Y	Y	Y	Y	

Y, Yes.

* Clinician factors include lack of interest, lack of referral.

had undergone 6-month epilepsy/EEG fellowship after general neurology training, none from Laos and Myanmar. The lack of expertise is also demonstrated in the distribution of the neurologists that have undergone EEG/epilepsy fellowship. There were 10 from Singapore with 5.6 million population, the same number as Indonesia with 261 million, Philippines (103 million) and Vietnam (93 million) and Thailand (69 million) (Table 1). Of the countries with large population (more than 50 million), Thailand stands out in having 5 out of 7 centers of level 4, as compared to Indonesia, Philippines, Vietnam and Myanmar (Table 2). Dedicated training in epilepsy surgery is essential for level 4 epilepsy center. Four countries offer subspecialty training in epilepsy (Thailand, Malaysia, Philippines, and Singapore), which may explain the accumulation of experts and establishment of more advanced epilepsy services in these countries, as compared to certain countries which provide only general neurology training such as Vietnam and Myanmar [21,27,28]. Greater opportunities to train in

established epilepsy surgery centers would help to overcome the under-development of epilepsy services in this region.

4.2. Facilities

Facilities for initial epilepsy pre-surgical evaluation (routine and sleep EEG, and MRI brain) are available in most countries. For lesional cases, surgery can be performed whenever the localizations of seizure semiology, interictal EEG and neuroimaging are concordant.²⁹ Advanced non-invasive (SPECT/ PET) and invasive investigations are available in only 45% of the ASEAN countries. The lack of facilities such as advanced investigations and high-quality MRI, as well as the lack of expert familiar with these epilepsy neuroimaging, limits the number of surgery especially for MRI-negative cases. In the smaller countries with < 20 million population (e.g., Brunei, Cambodia, Laos, Singapore, East Timor), more advanced epilepsy services are only available in Singapore which has adequate funding and facilities. However, in larger and economically under-developed countries, more specialized epilepsy services can still be developed as in Thailand and Malaysia if the resources are concentrated and organized. In Indonesia, lack of facilities is still a major barrier to development of more advanced epilepsy services [20].

4.3. Funding

Funding remained as the major limiting factor in most countries (73%) even in high income countries such as Brunei and Singapore. Despite high national GDP's, individual patients may be restrained by limited resources, particularly in paediatric patients whose families lack financial reserves. Dual health care systems in the region which comprise public and private hospitals lead to disparities in epilepsy surgery service. Public hospitals depend greatly on government budget allocation to provide affordable healthcare services and facilities to the general population. Low-income countries in the region are therefore unable to establish epilepsy center equipped with advanced pre-surgical investigation facilities and invasive monitoring. In certain countries such as Vietnam and Myanmar where healthcare services are not subsidized by the healthcare system and most of the population have no medical insurance [28], the cost of surgery will be borne by the patients. In contrast to public hospital, the costs of presurgical evaluation and surgery are exceptionally high in private hospitals. In countries such as Indonesia and Philippines where overall estimated costs of epilepsy surgery is 2.8 and 5.5 times higher than the nation's annual GDP per capita respectively, epilepsy surgery is affordable only in a small number of patients despite the availability of the facilities and service. The public/private healthcare divide can also lead to loss of trained epileptologists/epilepsy neurosurgeons to the private sector.

4.4. Other factors

Lack of referral by general neurologists and physicians is reported as a concern in 4 countries. This may be due to uncertainties about the definition of drug-resistant epilepsy and eligibility criteria for epilepsy surgery, as previously reported in survey of the attitude towards epilepsy surgery among clinicians or neurologists in other regions. [27–29] However, this might be also related to healthcare-system-related factors, e.g. lack of funding, facilities and expertise in the country, worries by private physicians of loss of income or patient factors such as fear of surgery and complications. Referral for assessment is indicated to determine who is drug-resistant and should go for epilepsy surgery in a timely fashion. Low thresholds for referral and measured, objective assessment for epilepsy surgery are required, which may be again limited by resources and specialist time. These clinician and patient factors need further exploration in future study.

4.5. Future implications

In this region with mostly lower-middle-income countries, development of a cost-effective evaluation system equipped with basic investigations including video-EEG and brain MRI, as proposed by Asadi-Pooya et al., will enable more potential surgical candidates to benefit from epilepsy surgery [29]. In addition, this study implies the need to train more clinicians and surgeons in the field of epilepsy surgery, as well as to promote the awareness of epilepsy surgery in this region. For challenging cases which require advanced investigations or invasive monitoring, sharing of resources within the region or advanced epilepsy training are recommended. Debate may arise over which aspects to prioritize, whether to concentrate on minimum level of epilepsy care or focus on building up tertiary epilepsy services. This study did not aim to prioritize high end epilepsy surgery assessment for refractory cases and devalue the need of physician and patient education to provide timely, accurate and effective diagnosis and treatment for all patients with epilepsy. Ultimately a two-fold approach may prove necessary. Broad-based basic care is required to ensure all persons with epilepsy receive the minimum standard and to permit identification of those with drug-resistant epilepsy. In addition, tertiary epilepsy services are required to reduce morbidity in those with drug-resistant epilepsy and deal definitively with their cases, thereby reducing the load on patient/caregivers and center. The existence of tertiary epilepsy services may be of indirect benefit by increasing confidence in the center and treatments used.

5. Conclusion

Epilepsy surgery is underutilized in ASEAN as evidenced by lack of epilepsy surgery centers and personnel, and limited availability of advanced presurgical evaluation. This is limited by lack of expertise, facilities and funding, as well as clinician- and patient-related factors.

Declarations of interest

We wish to confirm that there are no known conflicts of interest associated with this publication.

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