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Causes of death in patients with status epilepticus

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ABSTRACT

Background: Status epilepticus (SE) is a neurological disorder that affects to the high mortality risk. Several studies reported predictors of mortality in SE; actual causes of death in hospital and out of hospital are limited. This study aimed to describe the case fatality and the causes of death in patients with SE.
Methods: This was a descriptive study using the data collected in the national data of the Universal Coverage Scheme in Thailand during the fiscal year 2005 to 2015. Patients who admitted to hospitals and diagnosed as SE were included. The vital status of patients with SE was linked with the Ministry of the Interior and was classified into three phases: in-hospital, short-term, and long-term.
Results: Among 24,802 patients with SE, 1861 (7.5%) died in hospital, 1910 (7.7%) died within 30 days after hospital discharge, and 4906 (19.8%) died after 30 days. In-hospital death, SE complications (45.9%), seizure (19.6%), and comorbidities (15.4%) were the three common causes of death. While the common causes in short-term and long-term mortality were SE complications (27.7% and 31.0%), comorbidities (28.1% and 26.7%), and other causes (22.4% and 21.9%).
Conclusion: Status epilepticus complications and comorbidities were the common cause of death in patients with SE for all of three periods.
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1. Introduction

Status epilepticus (SE) is a neurological disorder with high mortality rate. A previous meta-analysis found that the pooled incidence rate was 12.6 per 100,000 person-years (95% confidence interval (CI) of 10.0 to 15.3). The pooled case fatality rate was 14.9% (95% CI: 11.7% to 18.7%) and higher in developing counties (15.6%, 95% CI: 13.0% to 18.6%) [1]. Previous studies showed that the in-hospital mortality rate was up to 44.0% [2–9]. The mortality rate after hospital discharge was slightly lower than the in-hospital mortality rate at 15.8%–31.5% [5,10–12].

Several studies reported mainly predictors for both short- and long-term mortality [10,13–16]. The study from Serbia found that older age or progressive symptom increased risk of death within the 30-day period with a coefficient of 1.05 and 15.6, respectively [13]. While another study found that children with convulsive SE are more prominent in nonseizure-related deaths [14]. Most studies were conducted in a small scale or tertiary care facilities. Additionally, there is limited data on details of causes of death in long period in a large SE population. This study aimed to describe causes of death in patients with SE by using a national database.

2. Material and methods

This study was a descriptive study and conducted on the Thai Universal Coverage Scheme electronic database. The Thai Universal Coverage Scheme is a basic insurance of Thai citizen and covered over 75% of Thai population. The inclusion criteria were patients diagnosed as SE and admitted to the hospital during the fiscal years of 2005 and 2015 (October 1, 2004 to September 30, 2015). The database search was performed by using the International Statistical Classification of Diseases and Related Health Problems – 10th Revision (ICD-10) code G41 (SE) with no restriction on age and gender. The patients with incomplete and erroneous data were excluded from this study.

All eligible patients were followed for at least one year; until September 30, 2016. Any death during the follow-up period was defined as the primary outcome. Deaths were identified by using the database

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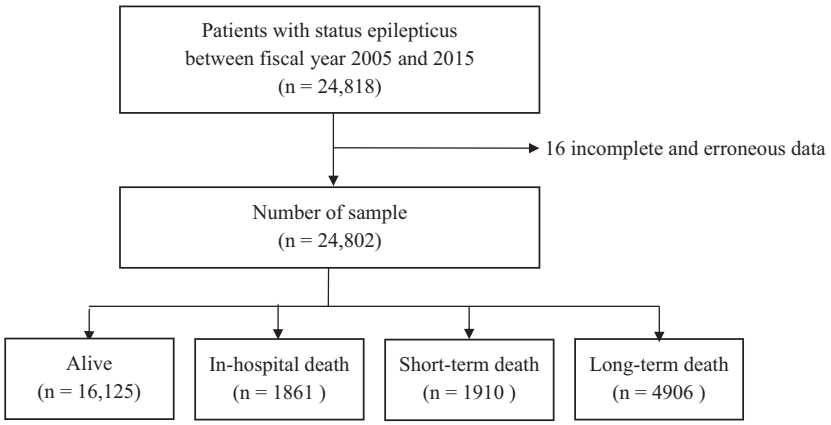

Fig. 1. Study flow.

of the Ministry of Interior. Causes of death were identified by death certificate and categorized into six categories: seizure or SE-related, SE complications, comorbidities, accidents, suicide, and other causes. Deaths were also categorized into three groups by time period of deaths as in-hospital, short-term, and long-term groups. Those who died during hospital admission were categorized as in-hospital group while those who died within or after 30 days of hospital discharge were labeled as short- and long-term group, respectively. The top three causes of death in overall were tabulated with the time period of deaths. Data were presented as frequency, percentage, and 95% CI. All statistical analyses were performed by using STATA software version 10.1 (College Station, Texas, USA). The study protocol was approved by the ethic committee in human research, Khon Kaen University, Khon Kaen, Thailand (HE622158).

3. Results

During the study period, there were 24,818 patients with SE who met the study criteria. Of those, 16 patients were excluded because of incomplete data. In total, there were 24,802 patients remaining in the final analysis. The median age of all patients was 36 years with a range of 0 to 99 years. Male sex accounted for 63.1%. The overall mortality rate was 35.0% (8677 patients) categorized as in-hospital death (7.5%; 1861 patients); short-term death (7.7%; 1910 patients); and long-term death (19.8%; 4906 patients) as shown in Fig. 1. In overall, the top three causes of death in patients with SE were deaths from SE complications (2903 patients), deaths from comorbidities (2134 patients), and deaths from other causes (1605 patients) as shown in Table 1. Deaths from SE complications were also the highest in in-hospital (n = 855) and long-term deaths (n = 1519) while deaths from comorbidities were the highest in short-term death (n = 536).

Regarding deaths from complications of SE, 18 causes were identified (Table 2). The top two causes of deaths from SE complications were septicemia (33.5%) and pneumonia (26.2%). These two causes were ranked as the first and second most common causes in in-hospital, short-term, and long-term deaths. There were 30 comorbidities identified as causes of death in patients with SE (Table 3). Cerebrovascular disease was the most common cause of death in patients with SE in overall (n = 665; 31.2%), in-hospital (n = 131; 45.8%), short-term (n = 166; 31.0%), and long-term (n = 368; 28.0%) categories. For other causes of death group, 18 causes were recorded (Table 4). Of those, deaths from senile cause was highest in overall (n = 836; 52.1%), short-term (n = 277; 64.7%), and long-term (n = 555; 51.7%). For the in-hospital deaths, cardiovascular collapse was the most common cause of death in this group (n = 65; 62.5%).

4. Discussion

The in-hospital fatality rate in this study was comparable from the previous national study from Taiwan (7.5% vs 8.81%) [2] and the US (7.5% vs 7.9–10.3%) [9]. The in-hospital mortality was high in children and the elderly population [2,5,8]. In those with age over 60 years, the fatality rate may be as high as 13.96% [2]. The short-term and long-term mortality rates in this study were lower than previous reports [5, 10–12]. The short-term mortality rate was lower than the previous reports for up to four times (7.7% vs 31.5%) [10,11] while the long-term mortality rate was somewhat lower than the previous reports (19.8% vs 21%) [5,12]. The explanations for these findings were sample size and causes of SE. In the previous studies, sample sizes were smaller than this study and included children and patients with SE with convulsive type or refractory type.

Table 1
Causes of death in patients admitted with status epilepticus (SE) during the fiscal years of 2005 and 2015 throughout Thailand.

Causes of death	In-hospital death (n = 1861)			Short-term death (n = 1910)			Long-term death (n = 4906)			Total (n = 8677)
	n	%	(95% CI)	n	%	(95% CI)	n	%	(95% CI)	
1. Seizure, SE	365	19.6%	(17.8%–21.5%)	134	7.0%	(5.9%–8.3%)	374	7.6%	(6.9%–8.4%)	873
2. Accidents	39	2.1%	(1.5%–2.9%)	53	2.8%	(2.1%–3.6%)	343	7.0%	(6.3%–7.7%)	435
3. Suicides	8	0.4%	(0.2%–0.8%)	2	0.1%	(0.01%–0.4%)	46	0.9%	(0.7%–1.2%)	56
4. SE complications	**855**	**45.9%**	**(43.7%–48.2%)**	529	27.7%	(25.7%–29.8%)	**1519**	**31.0%**	**(29.7%–32.3%)**	**2903**
5. Comorbidities	286	15.4%	(13.8%–17.1%)	**536**	**28.1%**	**(26.1%–30.1%)**	1312	26.7%	(25.5%–28.0%)	2134
6. Others	104	5.6%	(4.6%–6.7%)	428	22.4%	(20.6%–24.3%)	1073	21.9%	(20.7%–23.1%)	1605
7. Unknown	204	11.0%	(9.6%–12.5%)	228	11.9%	(10.5%–13.5%)	239	4.9%	(4.3%–5.5%)	671

Note. Bold indicated the highest number in column; CI: confidence interval; short-term death defined by deaths within 30 days after hospital discharge; long-term death defined by deaths 30 days after hospital discharge.

Table 2
Causes of death in patients admitted with status epilepticus (SE) during the fiscal years of 2005 and 2015 throughout Thailand from complications of SE (n = 2903).

SE complications	In-hospital death (n = 855)		Short-term death (n = 529)		Long-term death (n = 1519)		Total (n = 2903)	
Septicemia	340	(39.8%)	143	(27.0%)	489	(32.2%)	972	(33.5%)
Pneumonia	210	(24.6%)	120	(22.7%)	432	(28.4%)	762	(26.2%)
Acute renal failure	50	(5.8%)	94	(17.8%)	98	(6.5%)	242	(8.3%)
Respiratory failure	51	(6.0%)	47	(8.9%)	129	(8.5%)	227	(7.8%)
Cardiorespiratory failure	56	(6.5%)	21	(4.0%)	134	(8.8%)	211	(7.3%)
Encephalitis	44	(5.1%)	57	(10.8%)	40	(2.6%)	141	(4.9%)
Anoxic brain damage	49	(5.7%)	19	(3.6%)	58	(3.8%)	126	(4.3%)
Pulmonary edema	8	(0.9%)	6	(1.1%)	46	(3.0%)	60	(2.1%)
Cardiac arrhythmias	17	(2.0%)	6	(1.1%)	26	(1.7%)	49	(1.7%)
Cerebral edema	11	(1.3%)	9	(1.7%)	17	(1.1%)	37	(1.3%)
Airway obstruction	5	(0.6%)	2	(0.4%)	28	(1.8%)	35	(1.2%)
Urinary tract infection	8	(0.9%)	0	(0.0%)	17	(1.1%)	25	(0.9%)
Brain death	10	(1.2%)	6	(1.1%)	6	(0.4%)	22	(0.8%)
Acidosis	7	(0.8%)	3	(0.6%)	4	(0.3%)	14	(0.5%)
Hypoglycemia	2	(0.2%)	5	(0.9%)	6	(0.4%)	13	(0.4%)
SE complication (not identified)	2	(0.2%)	0	(0.0%)	4	(0.3%)	6	(0.2%)
Hyperglycemia	0	(0.0%)	0	(0.0%)	4	(0.3%)	4	(0.1%)
Injuries of head	1	(0.1%)	0	(0.0%)	2	(0.1%)	3	(0.1%)

Note. Data presented as number (%); some patients had more than one cause of death; short-term death defined by deaths within 30 days after hospital discharge; long-term death defined by deaths 30 days after hospital discharge.

In overall, we found that SE complications and comorbidities were the two most common causes of deaths in all three phases in this study (Table 1). These results were similar to the previous studies [13,14,16]. As previously reported, the main cause of death from SE was not SE-related but from SE complications [14]. Septicemia was the most common SE complication cause of death while cerebrovascular disease was the most common comorbidity contributing to deaths in patients with SE. Previous reports found that cerebrovascular disease was a common cause of SE [17–19] and increased risk of death by 3.56 times [12]. For septicemia, the mortality of SE was as high as 28% in combination of these two conditions [20]. For other causes of death, sudden cardiovascular collapse from an unknown cause was the most common cause in in-hospital setting while deaths from senile condition or unidentified condition were the most common cause of deaths after hospital discharge (Table 4). These results may be due to large proportion of the elderly patients in this study (41%; data not shown).

The strength in this study was the character of the study population. The enrollment from the Universal Coverage Scheme database made

Table 3
Causes of death in patients admitted with status epilepticus (SE) during the fiscal years of 2005 and 2015 throughout Thailand from comorbidities (n = 2134).

Comorbidities	In-hospital death (n = 286)		Short-term death (n = 536)		Long-term death (n = 1312)		Total (n = 2134)	
Cerebrovascular disease	131	(45.8%)	166	(31.0%)	368	(28.0%)	665	(31.2%)
Neoplasms	22	(7.7%)	50	(9.3%)	203	(15.5%)	275	(12.9%)
Diabetes mellitus	10	(3.5%)	66	(12.3%)	103	(7.9%)	179	(8.4%)
Neoplasms of brain	9	(3.1%)	37	(6.9%)	103	(7.9%)	149	(7.0%)
Pulmonary disease	11	(3.8%)	41	(7.6%)	76	(5.8%)	128	(6.0%)
Hypertension	7	(2.4%)	32	(6.0%)	76	(5.8%)	115	(5.4%)
Heart disease	22	(7.7%)	28	(5.2%)	56	(4.3%)	106	(5.0%)
Cirrhosis of liver	14	(4.9%)	24	(4.5%)	66	(5.0%)	104	(4.9%)
Dementia	0	(0.0%)	31	(5.8%)	71	(5.4%)	102	(4.8%)
Tuberculosis	18	(6.3%)	16	(3.0%)	32	(2.4%)	66	(3.1%)
Asthma	5	(1.7%)	16	(3.0%)	33	(2.5%)	54	(2.5%)
Cerebral palsy	8	(2.8%)	2	(0.4%)	39	(3.0%)	49	(2.3%)
Alcohol abuse	12	(4.2%)	5	(0.9%)	24	(1.8%)	41	(1.9%)
HIV disease	6	(2.1%)	9	(1.7%)	17	(1.3%)	32	(1.5%)
Deformations	2	(0.7%)	6	(1.1%)	22	(1.7%)	30	(1.4%)
Comorbidities (not identified)	0	(0.0%)	0	(0.0%)	19	(1.4%)	19	(0.9%)
SLE	7	(2.4%)	4	(0.7%)	5	(0.4%)	16	(0.7%)
Chronic kidney disease	0	(0.0%)	5	(0.9%)	10	(0.8%)	15	(0.7%)
Anemia	1	(0.3%)	3	(0.6%)	4	(0.3%)	8	(0.4%)
Intestinal obstruction	0	(0.0%)	1	(0.2%)	5	(0.4%)	6	(0.3%)
Helminths of nervous system	2	(0.7%)	1	(0.2%)	2	(0.2%)	5	(0.2%)
Disorders of skin	0	(0.0%)	3	(0.6%)	0	(0.0%)	3	(0.1%)
Allergy	0	(0.0%)	1	(0.2%)	1	(0.1%)	2	(0.1%)
Hyperlipidemia	0	(0.0%)	0	(0.0%)	2	(0.2%)	2	(0.1%)
Parkinson's disease	0	(0.0%)	0	(0.0%)	2	(0.2%)	2	(0.1%)
Schizophrenia	1	(0.3%)	0	(0.0%)	1	(0.1%)	2	(0.1%)
Gout	0	(0.0%)	1	(0.2%)	1	(0.1%)	2	(0.1%)
Muscle spasm	0	(0.0%)	0	(0.0%)	1	(0.1%)	1	(0.05%)
Poliomyelitis	0	(0.0%)	0	(0.0%)	1	(0.1%)	1	(0.05%)
Hyperthyroidism	0	(0.0%)	0	(0.0%)	1	(0.1%)	1	(0.05%)

Note. Data presented as number (%); some patients had more than one cause of death; short-term death defined by deaths within 30 days after hospital discharge; long-term death defined by deaths 30 days after hospital discharge; HIV: human immunodeficiency viruses; SLE: systemic lupus erythematosus.

Table 4
Causes of death in patients admitted with status epilepticus (SE) during the fiscal years of 2005 and 2015 throughout Thailand from other causes (n = 1605).

Others*	In-hospital death (n = 104)		Short-term death (n = 428)		Long-term death (n = 1073)		Total (n = 1605)	
Senile	4	(3.8%)	277	(64.7%)	555	(51.7%)	836	(52.1%)
Cardiovascular collapse	65	(62.5%)	110	(25.7%)	345	(32.2%)	520	(32.4%)
Infectious causes	16	(15.4%)	13	(3.0%)	73	(6.8%)	102	(6.4%)
Gastroesophageal laceration-hemorrhage	5	(4.8%)	6	(1.4%)	27	(2.5%)	38	(2.4%)
Shock	8	(7.7%)	3	(0.7%)	10	(0.9%)	21	(1.3%)
Acute hepatic failure	3	(2.9%)	2	(0.5%)	11	(1.0%)	16	(1.0%)
Hepatitis	1	(1.0%)	4	(0.9%)	9	(0.8%)	14	(0.9%)
Disorders of mineral metabolism	0	(0.0%)	4	(0.9%)	8	(0.7%)	12	(0.7%)
Sudden unexpected death syndrome	0	(0.0%)	0	(0.0%)	10	(0.9%)	10	(0.6%)
Acute nephritic syndrome	1	(1.0%)	1	(0.2%)	7	(0.7%)	9	(0.6%)
Assault	0	(0.0%)	0	(0.0%)	8	(0.7%)	8	(0.5%)
Mosquito-borne viral encephalitis	0	(0.0%)	5	(1.2%)	1	(0.1%)	6	(0.4%)
Nutritional deficiencies	0	(0.0%)	0	(0.0%)	5	(0.5%)	5	(0.3%)
Malaria	1	(1.0%)	1	(0.2%)	1	(0.1%)	3	(0.2%)
Dengue fever	0	(0.0%)	1	(0.2%)	1	(0.1%)	2	(0.1%)
Acute peritonitis	0	(0.0%)	0	(0.0%)	2	(0.2%)	2	(0.1%)
Pulmonary hemorrhage	0	(0.0%)	1	(0.2%)	0	(0.0%)	1	(0.1%)
Bee allergy	1	(1.0%)	0	(0.0%)	0	(0.0%)	1	(0.1%)

Note. Some patients had more than one cause of death; short-term death defined by deaths within 30 days after hospital discharge; long-term death defined by deaths 30 days after hospital discharge. * The causes of death that not relate to SE-direct (seizure, SE) and indirect causes (accidents, suicides, SE complications, comorbidities).

this study a large study population, multicenter, and multilevel. The database included primary, secondary, and tertiary care hospitals all over Thailand. Additionally, the vital status of patients were checked by the Ministry of Interior that gave a complete 100% of data completion. However, there were some limitations in this study. First, the cause of death in each patient was identified by the death certificate. In Thailand, if the patients died out-of-hospital with natural death, the definitive cause of death would not be identified. In addition, we lacked details of severity of SE and treatment that were the important information related to death in patients with SE.

5. Conclusions

The main causes of death in patients with SE were SE complications and comorbidities in in-hospital or after discharge. The SE or SE-related cause of death was high in in-hospital setting.

Declaration of Competing Interest

All authors declare no competing interests.

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