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# Predictors of long-term mortality in status epilepticus

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# ABSTRACT

*Background:* There were several studies that have reported on the long-term mortality rate of status epilepticus (SE). However, these studies were conducted mainly in Western countries using small study populations. This study aimed to evaluate predictors for long-term mortality in SE using the Thai national healthcare database. *Methods:* This study was conducted using the Thai national Universal Health Coverage (UC) database. The eligibility criteria for this study were that all patients were diagnosed with SE and had been admitted to any hospital between 2005 and 2015. Mortality was defined at discharge and at one, three, five, and 10 years. All eligible patients were categorized as either having survived or having died. The mortality rates were calculated at one, three, five, and 10 years. Factors associated with mortality were analyzed using backward multivariate Cox proportional hazard regression analysis. Kaplan–Meier was performed to estimate the survival rate.

*Results*: During the study period, there were 21,732 patients with SE admitted who met the study criteria. The total observation time was 85,821.28 person-years. Of the patients enrolled, 3642 (or 4.24 per 100 person-years [95% confidence interval (CI): 4.11–4.38]) died. Factors positively associated with mortality in patients with SE were central nervous system (CNS) infection, cancer, heart diseases, chronic renal failure, septicemia, pneumonia, respiratory failure, acute renal failure, and shock. Heart diseases had the highest adjusted hazard ratio at 2.69 (95% CI: 2.47–2.93). Two factors were negatively related with SE mortality: hypertension and urinary tract infection.

*Conclusion:* Long-term mortality in patients with SE had both positive and negative predictors in the national database.

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## 1. Introduction

Status epilepticus (SE) is an emergency neurological condition that carries a high mortality risk. The annual SE incidence rate ranges from 1.84 to 42.0 per 100,000 population. This number is higher in populations at extreme ends of the age spectrum: children and elderly patients [1–6]. Although SE is more common in patients with epilepsy, the mortality risk is higher in patients with SE without epilepsy. The hazard ratio for mortality of SE in patients without history of epilepsy is 1.61 while in patients with SE with a prior history of epilepsy, it is 1.16 [7]. The overall SE mortality rate varies between 24.9% and 29.2% [7]. This rate is dependent on several factors, but comorbid conditions and complications are the major factors that increase this risk [5,8–14].

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There have been at least four studies that have reported on the longterm mortality rate of SE [15–18]. The average 10-year mortality rate of patients with SE has been reported as being 43%, a number that can be as high as 82% in elderly patients [16]. Risk factors associated with long-term mortality in patients with SE are SE lasting more than 24 h, acute symptomatic SE, and myoclonic SE, the relative mortality risks of which were 2.3, 2.2, and 4.0, respectively [17]. However, these studies were conducted mainly in Western countries using small study populations. This study aimed to evaluate predictors for long-term mortality in SE using the Thai national healthcare database.

# 2. Materials and methods

This study was a retrospective cohort study conducted using the Thai national Universal Health Coverage (UC) database which covers approximately 75% of Thai citizens. The eligibility criteria for this study were that all patients were diagnosed with SE and had been admitted to any hospital between 2005 and 2015. We searched on the





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UC database using the International Classification of Diseases, Tenth Edition (ICD-10), code G41 for SE.

Clinical data of all eligible patients were retrospectively reviewed. Mortality was defined by at last discharge status or after discharged within 30 days and data was defined as censoring if patient was still alive at the end of the study. The mortality data were retrieved from the Ministry of the Interior database. Note that death was defined as all-cause mortality.

We searched for all studied variables using the UC database. The following ICD-10 codes were used in this search: central nervous system (CNS) infections (A06.6, A17, A39, A80–A89, B00.3, B00.4, B01.1, B02.0, B02.1, B05.0, B05.1, B06.0, B22.0, B26.1, B26.2, B37.5, B38.4, B43.1, B50.0, B58.2, B60.2, G00–G09, R29.1), cancer (C00–C97), brain tumor (C71, D33, D43), anemia (D50–D64), diabetes (E10–E14), hypertension (I10–I15), heart diseases (I05–I09, I27, I30–I52), ischemic heart diseases (I20–I25), cerebrovascular diseases (I60–I69), chronic renal failure (N18), septicemia (A40–A41, R50), pneumonia (J12–J18), respiratory failure (J96), acute renal failure (N17), urinary tract infection (N39.0), and shock (R57).

All eligible patients were categorized as either having survived or having died. The mortality rates were calculated at one, three, five, and 10 years. Factors associated with mortality were analyzed using both univariate and backward multivariate Cox proportional hazard regression analysis. Kaplan–Meier was performed to calculate the survival rate. All analyses were performed using STATA software (version 10.0, College Station, Texas, USA).

#### 3. Results

During the study period, there were 21,732 patients with SE admitted who met the study criteria. The total observation time was 85,821.28 person-years. Of the patients enrolled, 3642 (or 4.24 per 100 person-years [95% confidence interval (CI): 4.11–4.38]) died. The survival rate within one, three, five, and 10 years of first admission were 83.5% (95% CI: 83.0%–84.0%), 83.3% (95% CI: 82.7%–83.9%), 83.2% (95% CI: 82.7%–63.7%), and 83.0% (95% CI: 82.5%–83.5%), respectively (Fig. 1).

The average age of all patients was 36.37 years (standard deviation (SD): 25.78). Most patients were male (63.1%). The three most common conditions were respiratory failure (20.9%), cerebrovascular disease (15.1%), and pneumonia (14.3%), as shown in Table 1.

The conditions which were significantly associated with mortality after adjustment for age and gender are shown in Table 2. Factors positively associated with mortality in patients with SE were CNS infection, cancer, heart diseases, chronic renal failure, septicemia, pneumonia,

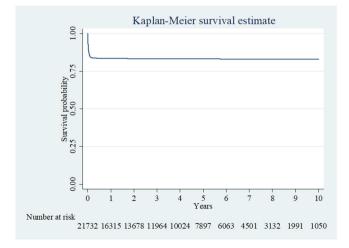


Fig. 1. Probability of survival in patients with status epilepticus over a 10-year study period.

## Table 1

Characteristics of admitted patients with SE according to the national database.

Characteristic	Number	Percentage
Female	8,019	36.9%
Age (years)		
<10	5324	24.5%
11-20	1824	8.4%
21-30	2041	9.4%
31-40	2576	11.8%
41-50	2892	13.3%
51-60	2469	11.4%
>60	4606	21.2%
CNS infection	441	2.0%
Cancer	242	1.1%
Brain tumor	139	0.6%
Anemia	1822	8.4%
Diabetes	1572	7.2%
Hypertension	2664	12.3%
Heart diseases	1312	6.0%
Ischemic heart disease	312	1.4%
Cerebrovascular disease	3271	15.1%
Chronic renal failure	656	3.0%
Septicemia	1760	8.1%
Pneumonia	3102	14.3%
Respiratory failure	4550	20.9%
Acute renal failure	880	4.0%
Urinary tract infection	1137	5.2%
Shock	608	2.8%

respiratory failure, acute renal failure, and shock. Heart diseases had the highest adjusted hazard ratio at 2.69 (95% CI: 2.47–2.93). Two factors were negatively related with SE mortality: hypertension and urinary tract infection (Table 2).

#### 4. Discussion

This longitudinal cohort study found that the 10-year mortality rate of admitted patients with SE was 17%, which was lower than the 43% mortality rate found in a previous review [16]. Similar to the previous report, the mortality rate in our study was not specific to SE deaths but indicated all-cause mortality. A long-term cohort study in children with SE found that 75% of deaths in child patients with SE were not related to SE but occurred as a result of comorbid conditions [18]. The low mortality rate in this study may be due to the characteristics of the study population. All age ranges were included in the study, resulting in lower mortality than in previous reviews, which enrolled more adult patients. Children with SE usually have lower long-term mortality rate sthan adult patients (11% vs 43%) [16,18]. Note that the mortality rate after one year was quite steady (Fig. 1).

Two studies found that no significant comorbidities or clinical factors at the time of SE diagnosis were predictors for long-term mortality, either in children or elderly patients with SE [17,18]. In children, only

Table 2								
Significant factors associated with mortality in patients with SE and their incidence rates.								
Factors	Number	ID/100	Crudo	Adjusted	OF% CI			

Factors	Number of deaths	IR/100	Crude HR	Adjusted HR	95% CI
CNS infection	150	10.41	1.81	2.13	1.80-2.52
Cancer	96	14.76	1.64	1.72	1.40-2.11
Hypertension	812	10.72	1.60	0.86	0.79-0.94
Heart diseases	779	33.88	4.23	2.69	2.47-2.93
Chronic renal failure	331	30.26	2.73	1.78	1.58-2.00
Septicemia	836	20.47	3.20	2.26	2.08-2.45
Pneumonia	934	9.23	2.12	1.18	1.09-1.28
Respiratory failure	1524	13.46	2.49	1.69	1.58-1.82
Acute renal failure	566	46.10	4.31	2.16	1.95-2.38
Urinary tract infection	352	9.72	1.35	0.83	0.74-0.94
Shock	458	97.05	5.26	2.33	2.09-2.60

Note. CNS: central nervous system; IR/100: incidence rate per 100 person-years; HR: hazard ratio; 95% CI: 95% confidence interval.

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