

Abstract

Introduction: New-onset refractory status epilepticus (NORSE) occurs in patients without prior epilepsy or relevant neurological conditions, characterized by refractory status epilepticus without a clear cause upon initial evaluation. Cryptogenic NORSE is diagnosed when no cause is identified after extensive evaluation. This study investigates prognostic factors and long-term outcomes in cryptogenic NORSE patients treated at the Neurological Institute of Thailand.

Objective: To compare clinical and demographic variables between patients with favorable ($mRS < 3$) and unfavorable ($mRS \geq 3$) outcomes at 12 months post-onset and identify factors influencing treatment efficacy.

Material and Method: A retrospective cohort study using medical records from June 1, 2016, to October 15, 2023. Patients were classified as cryptogenic NORSE based on inclusion and exclusion criteria. Clinical and demographic variables and treatment outcomes were assessed through medical records and telephone interviews. Statistical analysis was performed using SPSS.

Results: Out of 153 patients with status epilepticus, 20 met the criteria for cryptogenic NORSE. Nine patients (45%) had favorable outcomes ($mRS < 3$), and 11 (55%) had unfavorable outcomes ($mRS \geq 3$). Lower CSF white blood cell count (unfavorable group median 3.0 cells/cu.mm compared to favorable group median 8.0 cells/cu.mm, $p = 0.023$) and higher anesthetic drug use (unfavorable group median 3.0 compared to favorable group median 1.0, $p = 0.006$) were significant predictors of poor outcomes. Mortality was 30% (6/20), primarily due

Predictor of Outcome in Cryptogenic New-onset Refractory Status Epilepticus

Peerapon Watchalayann,
Metha Apiwattanakul,
Saharat Aungsumart

Peerapon Watchalayann,
Metha Apiwattanakul,
Saharat Aungsumart

Department of Neurology, Neurological Institute of Thailand

Corresponding author:
Saharat Aungsumart, M.D. PhD.

Department of Neurology, Neurological Institute of Thailand, 312,
Thung Phaya Thai, Ratchatewi, Bangkok 10400, Thailand
Tel. : 66-2306-9899
e-mail: saharatau@nit.go.th

to infections, with survivors (14/20) experiencing epilepsy (100%), memory impairment (71%), and psychiatric issues (21%).

Conclusion: Cryptogenic NORSE is associated with high morbidity and mortality. However, approximately 50% of patients may achieve a favorable functional outcome. Factors associated with poor prognosis include lower CSF white blood cell counts and a higher number of anesthetic agents used.

Keywords: New-onset refractory status epilepticus, Cryptogenic new-onset refractory status epilepticus, NORSE, Cryptogenic NORSE predictor, Febrile infection-related epilepsy syndrome, outcome

Introduction

New-onset refractory status epilepticus (NORSE) presents in patients without prior epilepsy or relevant neurological conditions, characterized by refractory status epilepticus without a clear structural, toxic, or metabolic cause. When no cause is identified after extensive evaluation, the condition is termed cryptogenic NORSE.¹ Mortality rates for NORSE range from 22-30%.¹ Most NORSE cases are linked to autoimmune diseases, paraneoplastic syndromes, or infections, yet 50-60% remain unexplained.² Febrile infection-related epilepsy syndrome (FIREs) is a subset of NORSE, defined by fever occurring within two weeks before refractory status epilepticus (RSE) onset. The estimated incidence of NORSE and FIREs is 1:100,000 to 1:1,000,000.^{3,4}

The etiology and mechanisms underlying cryptogenic NORSE remain unclear, though evidence suggests brain inflammation, supported by elevated cytokine levels, particularly IL-6, in cere-

brospinal fluid.^{5,6} Treatment lacks standardization, relying on immunotherapy with methylprednisolone, IVIG, or plasma exchange.⁷ Additional therapies include Rituximab, cyclophosphamide, and Tocilizumab.⁷ Despite aggressive treatment, outcomes are often poor.^{8,9} Mortality rates for NORSE and FIREs remain high, with rates of 12% in children and 16-27% in adults. Survivors frequently suffer from epilepsy, cognitive impairment, and functional disability.¹⁰ In-hospital mortality for cryptogenic NORSE reaches 22%, with 67% of survivors having mRS ≤ 3 at discharge and 55% continuing to experience epilepsy.¹¹

Research on prognostic variables and long-term outcomes in cryptogenic NORSE is limited.¹¹⁻¹³ Uncertainty in long-term prognosis complicates patient counseling and treatment planning. This study aims to investigate the long-term treatment outcomes (1 year after onset) and identify factors affecting treatment outcomes and prognosis in cryptogenic NORSE patients treated at the Neurological Institute of Thailand.

Objective

The primary objective of this study is to compare clinical and demographic variables between patients with favorable treatment outcomes (mRS < 3 at 12 months post-onset) and those with unfavorable outcomes (mRS ≥ 3). This aims to identify factors influencing treatment efficacy and predict prognosis in cryptogenic New-Onset Refractory Status Epilepticus (NORSE) patients. The secondary objective is to collect comprehensive treatment outcome data for cryptogenic NORSE patients.

Materials and Methods

Study design and participant

We conducted a retrospective real-world observational cohort study using data from electronic and paper medical records from the Neurological Institute of Thailand database. We selected patients treated at the Neurological Institute from June 1, 2016, to October 15, 2023, who were diagnosed with status epilepticus (G.41). Patients were selected based on predefined inclusion and exclusion criteria to identify those meeting the definition of cryptogenic NORSE. The inclusion criteria required patients to have failed treatment with two or more antiepileptic drugs, demonstrated negative microbiologic studies of serum and/or cerebrospinal fluid (CSF) ruling out infection, and showed no autoimmune etiology based on a negative autoimmune neurologic antibody panel, which included anti-NMDAR, anti-GABAb, anti-DPPX, anti-LGI1, anti-CASPR2, ANNA-1, ANNA-2, ANNA-3, PCA-1, anti-GAD, anti-CRPM5, and anti-amphiphysin. These antibodies were screened using tissue indirect immunofluorescence, cell-based assays, or line blot techniques as appropriate. Additionally, patients were required to have normal metabolic panel results, MRI findings showing no structural abnormalities or tumors causing seizures, and no history of substance abuse or chemical exposure, or negative results for toxic substances in urine testing. Patients were excluded if they had a prior history of epilepsy or central nervous system diseases, were diagnosed with other diseases during follow-up, or had incomplete or

inaccessible medical records preventing adequate data collection. After identifying patients who met the criteria for cryptogenic NORSE, baseline characteristics and relevant clinical variables were recorded. In cases where direct data collection was not possible, treatment outcomes were obtained through telephone interviews. Patients were then divided into two groups: those with favorable treatment outcomes (mRS score < 3 at 12 months post-onset) and those with unfavorable treatment outcomes (mRS score \geq 3 at 12 months post-onset). Statistical analysis was conducted to identify predictor outcomes.

Statistical analysis

Demographic data and variable outcome, continuous variables were presented as the median and interquartile range, while categorical variables were described as percentages. Differences in baseline characteristics between favorable treatment outcomes (mRS < 3) and unfavorable treatment outcomes (mRS \geq 3) were analyzed using the Mann-Whitney U test for continuous variables and Fisher's Exact test for categorical variables. To identify predictor variables, a univariable logistic model was employed to examine the individual relationship between each variable and Poor outcome.

All probability values were two-sided, and the level of significance was set at p-values < 0.05. Statistical analyses were performed using SPSS for Windows version 16.0 (SPSS Inc., Chicago, Illinois, USA).

Results

Between June 1, 2016, and October 15, 2023, a total of 153 patients were diagnosed with status epilepticus at the Neurological Institute of Thailand. After applying the inclusion and exclusion criteria, 30 patients met the study requirements for cryptogenic new-onset refractory status epilepticus (cryptogenic NORSE). Due to missing in contacting patients or missing critical data, 10 patients were excluded, resulting in a final cohort of 20 patients included in this analysis. These patients were

subsequently classified into two groups based on treatment outcomes: those with favorable outcomes, defined as a modified Rankin Scale (mRS) score of less than 3 at 12 months post-onset ($n = 9$, 45%), and those with unfavorable outcomes, defined as an mRS score of 3 or greater ($n = 11$, 55%). Among the patients with unfavorable outcomes, 6 (55%) died, primarily due to infection-related complications

A flow diagram illustrating the selection process is presented in Figure 1.

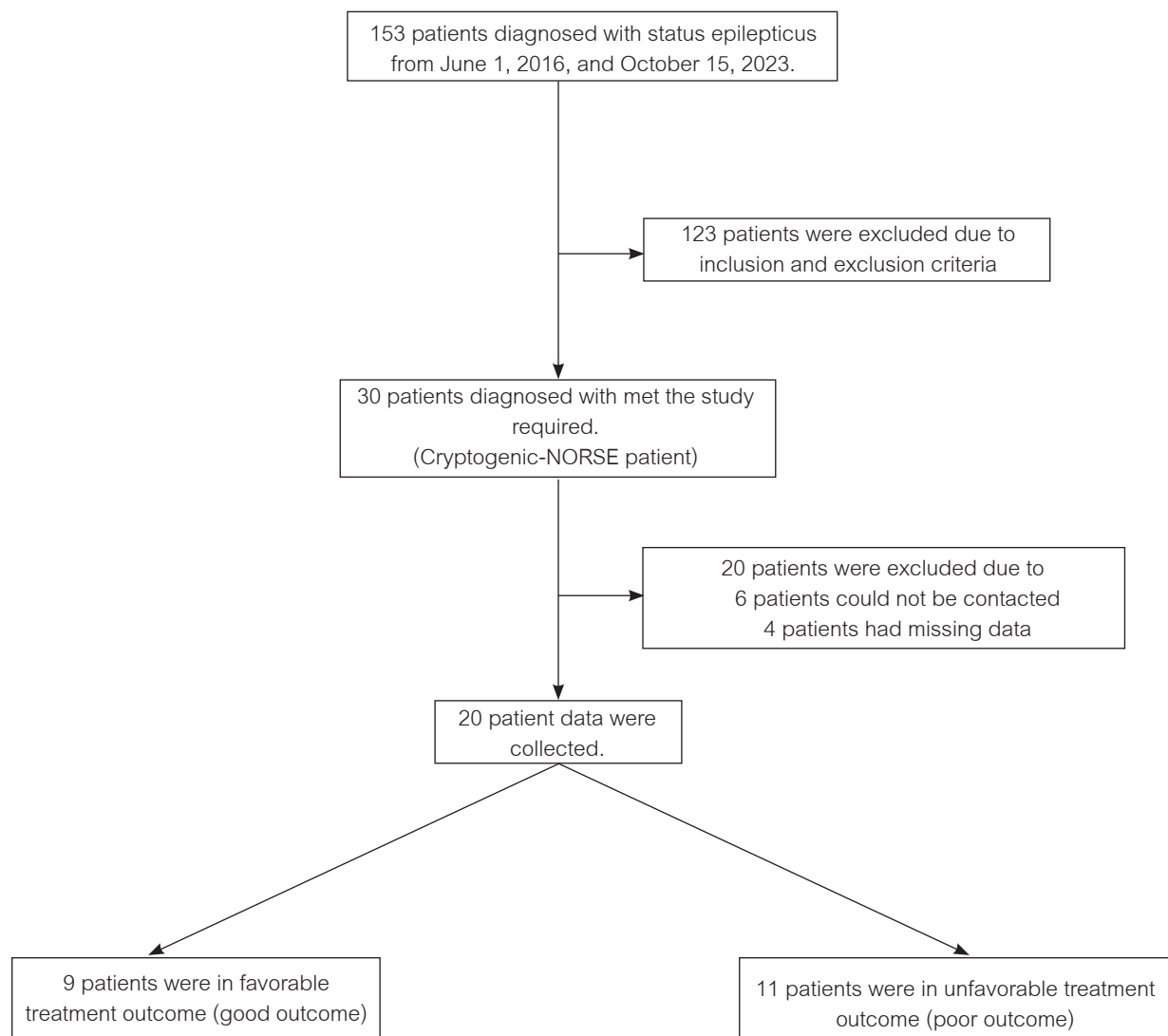


Figure 1. Flow diagram of Participant recruitment and retention.

Baseline Characteristics

Baseline characteristics are summarized in Table 1. Both groups were comparable, with minor, non-significant differences. The cohort's median age was 26.5 years (IQR: 20.2-35.5). Males comprised 50% of patients, with 95% presenting tonic-clonic seizures at onset. Fever occurred in 95%,

rising to 100% in the favorable outcome group vs. 90.9% in the unfavorable group. Behavioral changes were noted solely in the favorable outcome group (11.1%). Most patients (90%) had C-NORSE scores of 5-6, with all having a pre-onset mRS of 0. One patient had Type 1 Diabetes Mellitus as an underlying autoimmune condition.

Table 1 Baseline characteristics

Characteristics	Total (n = 20)	Outcome at 12 months		P
		Good (mRS < 3) (n = 9)	Poor (mRs ≥ 3) (n = 11)	
Sex (male) (N,%)	10 (50)	6 (66.7)	4 (36.4)	0.370
Age (year; median, IQR)	26.5 (20.2-35.5)	22.0 (19.5-42.5)	32.0 (21.0-34.0)	0.879
Symptom (N,%)				
Confusion	4 (20)	1 (11.1)	3 (27.3)	0.591
Fever	19 (95)	9 (100)	10 (90.9)	1
Headache	14 (70)	6 (66.7)	8 (72.7)	1
Upper respiratory tract symptom	4 (20)	1 (11.1)	3 (27.3)	0.591
Behavioral change	1 (5)	1 (11.1)	0.0	0.450
Myalgia	7 (35)	3 (33.3)	4 (36.4)	1
Seizure type at onset (N,%)				1
Tonic-clonic	19 (95)	9 (100)	10 (90.9)	
Complex partial	1 (5)	0.0	1 (9.1)	
Auto-antibody profile (N,%)				
Serum Anti-TPO	-	-	-	
Serum P-ANCA	-	-	-	
Serum C-ANCA	-	-	-	
Serum ANA	2 (25)	1 (25)	1 (25)	1
C-NORSE score 5-6 (N,%)	18 (90)	9 (100)	9 (81.8)	0.479
Underlying autoimmune disease (N,%)	1 (5)	0.0	1 (9.1)	1
mRS score before onset (median, IQR)	0	0, 0-0	0, 0-0	
Time from onset to last follow-up (month; median, IQR)	47.0 (15.5-79.5)	46.0 (27.0-85.5)	48.0 (12.0-80.0)	0.543

Predictors of Outcome

Predictor analysis was conducted to identify factors that might influence the outcomes at 12 months, as shown in Table 2.

Table 2 Predictor for poor outcome at 12 months

Factors	Outcome at 12 months		P
	Good (mRS < 3)	Poor (mRs ≥ 3)	
	(n = 9)	(n = 11)	
General clinical data			
Onset to tertiary hospital time (day; median, IQR)	9.0 (7-10)	12.0 (5-14)	0.303
Seizure type at onset (N,%)			1.000
Tonic-clonic	9 (100)	10 (90.9)	
Complex partial	0	1 (9.1)	
Duration stays in hospital (day; median, IQR)	41.0 (24.0-66.5)	34.0 (14-80)	0.970
Duration stays in ICU (day; median, IQR)	24.0 (18.5-56)	30.0, (14-59)	0.790
STESS score (median, IQR)	4.0 (3.5-4)	4.0, (4-4)	0.744
C-NOSE score (median, IQR)	5.0 (5-6)	5.0 (5-6)	0.701
Duration of last clinical seizure to onset (day; median, IQR)	29.0 (15-48)	34.0 (16-51)	0.909
Duration of last EEG seizure to onset (day; median, IQR)	14.0 (0-32)	18.0 (11-36)	0.515
CSF WBC (Cell/cu.mm; median, IQR)	8.0 (3.5-16.5)	3.0 (0.0-5.0)	0.023*
CSF RBC (Cell/cu.mm; median, IQR)	9.0 (0-206.5)	104.0 (0-177)	0.415
CSF protein (mg/dL; median, IQR)	23.0 (20-38)	45.0 (36-70)	0.074
CSF IL-6 (pg/ml; median, IQR)	56.0 (35.2-71)	110.5 (39.2-3438)	0.394
Serum IL-6 (pg/ml; median, IQR)	14.9 (8.9-14.9)	22.0 (13.5-27.2)	0.724
EEG seizure (N,%)	6 (66.7)	9 (81.8)	0.617
Generalized	1 (16.7)	1 (11.1)	
Unilateralized	2 (33.3)	4 (44.5)	
Bilateral independent	3 (50)	2 (22.2)	
Multifocal	0.0	2 (22.2)	
EEG background at onset (N,%)	9 (100)	11 (100)	0.157
Burst-suppression	1 (11.1)	5 (45.5)	
Suppressions	1 (11.1)	0.0	
Generalized slow	7 (77.8)	6 (54.5)	
MRI finding (N,%)			1.000
Normal		3 (33.3)	3 (27.3)
Abnormal		6 (66.7)	8 (72.7)

Factors	Outcome at 12 months		P
	Good (mRS < 3)	Poor (mRs ≥ 3)	
	(n = 9)	(n = 11)	
MRI finding (N,%)			
Limbic only	1 (16.7)	0.0	0.429
Bilateral limbic	5 (83.3)	4 (50)	0.301
Bilateral neocortical temporal lobe	0.0	1 (12.5)	1.000
Bilateral neocortical temporal lobe & limbic	0.0	2 (25)	0.473
Other lobe	3 (50)	7 (87.5)	0.245
Multifocal	0.0	1 (12.5)	1.000
Treatment			
Number of Anti-seizure medication (median, IQR)			
Number of types	5.0 (5-6.5)	6.0 (5-7)	0.504
Number of maximum uses simultaneously	5.0 (4.5-5.5)	6.0 (5-7)	0.177
Number of Anesthetics drug (median, IQR)			
Number of types	1.0, 1.0-2.5	3.0, 2.0-4.0	0.023 ^a
Number of maximum uses simultaneously	1.0, 1.0-2.0	3.0, 2.0-3.0	0.006 ^c
Duration of anesthetic use (day; median, IQR)	9.0 (3.5-24)	10.0 (5-30)	0.594
Time to start first immunotherapy from onset (day; median, IQR)	8.0 (4.5-11)	9.0 (4-13)	0.939
Immunotherapy (N,%)			
IV methylprednisolone	9 (100)	10 (90.9)	1.000
IV Rituximab	0.0	2 (18.2)	0.479
IV Tocilizumab	4 (44.4)	3 (27.3)	0.370
Plasma exchange	7 (77.8)	9 (81.8)	0.625
Cyclophosphamide	1 (11.1)	1 (9.1)	1.000
IVIg	0.0	9.1	0.550
IV Rituximab dose 2 (N,%)	0.0	3 (27.3)	0.218
IV Tocilizumab dose 2 (N,%)	2 (22.2)	3 (27.3)	1.000
Complication			
Nosocomial infection (N,%)	9 (100)	11 (100)	-
Serum ammonia level (micromole/L; median, IQR)	64.5 (58.2-133.3)	52.0 (36.5-86.5)	0.318
Hypotension need vasopressor (N,%)	4 (44.4)	7 (63.6)	0.653
Renal dysfunction (N,%)	0.0	4 (36.4)	0.094
Liver dysfunction (N,%)	7 (77.8)	5 (45.5)	0.197
Hyponatremia (N,%)	5 (55.6)	7 (63.6)	1.000
Hypernatremia (N,%)	3 (33.3)	6 (54.5)	0.406
Thrombocytopenia (N,%)	1 (11.1)	2 (18.2)	1.000
Intubation and ventilator need (N,%)	9 (100)	11 (100)	-
Duration of intubation and ventilator need (day; median, IQR)	29.0 (21.5-54)	39.0 (21-60)	0.648

Notably, cerebrospinal fluid (CSF) white blood cell count was found to be lower in the unfavorable outcome group, with a median of 3.0 cells/cu.mm (IQR: 0.0-5.0) compared to 8.0 cells/cu.mm (IQR: 3.5-16.5) in the favorable group, and this difference was statistically significant ($p = 0.023$). Additionally, the number of type anesthetic drugs administered was significantly higher in the unfavorable outcome group, with a median of 3.0 (IQR: 2.0–4.0) compared to a median of 1.0 (IQR: 1.0–2.5) in the favorable outcome group ($p = 0.023$). Furthermore, the maximum number of anesthetic drugs used simultaneously during treatment was also significantly greater in the unfavorable outcome group (median: 3.0, IQR: 2.0–3.0) compared to the favorable outcome group (median: 1.0, IQR: 1.0–2.0), demonstrating a statistically significant difference ($p = 0.006$).

Other clinical data or treatment factors and complication, including CSF and serum IL-6 level, duration of last EEG seizure to onset, time to start first immunotherapy from onset, and immunotherapy use such as IV Tocilizumab, did not demonstrate statistically significant differences between the groups.

Outcome of the overall cohort

Table 3 shows treatment outcomes over time. At six months post-onset, the cohort's median mRS was 4 (IQR: 3-5.75), indicating moderate to severe disability. By 12 months, the median mRS improved to 3 (IQR: 2-6). At the latest follow-up (median 47 months, IQR: 15.5-79.5), the median mRS was 2 (IQR: 2-6), suggesting a continuous, albeit gradual, recovery over time in patients with NORSE.

Mortality was high, with six patients (30%) succumbing to complications. Infections accounted for five of the six deaths, while arrhythmia caused one. The predominance of infection-related mortality aligns with the high rate of nosocomial infections during hospitalization.

Sequelae were prevalent among survivors, with all 14 surviving patients experiencing long-term complications. The most common sequelae included epilepsy (100%), memory impairment (71.4%), and psychiatric or behavioral disturbances (21.4%). This highlights the significant and lasting neurological burden associated with cryptogenic NORSE.

Table 3 Outcome

Characteristics	Total
mRS score at 6 month after onset (median, IQR)	4, 3-5.75
mRS score at 12 month after onset (median, IQR)	3, 2-6
mRS score at last follow-up (median, IQR)	2, 2-6
Time from onset to last follow-up (month; median, IQR)	47, 15.5-79.5
Mortality (case, percentage)	6, 30%
At hospital	5, 25%
After discharge	1, 5%
Cause of dead (case/total)	
Infection	5/6
Arrhythmia	1/6
Sequelae after disease (case/total)	
Epilepsy	14/14
Memory problem	10/14
Psychiatric and behavioral	3/14

Discussion

This study aimed to evaluate the outcomes of patients with cryptogenic NORSE. At 12 months of follow-up, 45% of patients achieved a favorable functional outcome, while 55% experienced poor outcomes. Among those with unfavorable outcomes, six patients (30%) succumbed, primarily due to hospital-acquired infections. Notably, survivors demonstrated continuous functional improvement over time, as indicated by the progressive decline in mRS scores from 6 to 12 months and at the final follow-up.

Two key factors were associated with unfavorable outcomes in this cohort: a low CSF WBC count and the use of a higher number of anesthetic agents. The greater use of anesthetic agents in the unfavorable outcome group likely reflects the increased severity of seizures and the challenges in achieving seizure control, which correlates with poorer neurological outcomes. While brain inflam-

mation is considered a central mechanism in NORSE pathogenesis^{1,5}, genetic predisposition has also been implicated in some cases^{10,14}. The lower CSF WBC count observed in patients with unfavorable outcomes may suggest a non-inflammatory mechanism, potentially driven by genetic factors contributing to seizure severity. However, genetic testing was not performed in this study, limiting further exploration of this hypothesis.

Interestingly, factors that have been reported to influence favorable outcomes in NORSE in previous studies include CSF or serum interleukin-6 (IL-6) levels, time to first immunotherapy, and the use of intravenous tocilizumab^{3,8,11,15}. Contrary to expectations, the unfavorable outcome group in this study exhibited a trend toward higher CSF and serum IL-6 levels, as well as delayed initiation of immunotherapy. This observation suggests that elevated IL-6 levels and delayed treatment may be associated with worse outcomes. However, the small sample size in this study may have limited the statistical

power to detect significant differences. Further research with larger cohorts is warranted to clarify the impact of these factors on NORSE outcomes.

NORSE remains a condition with high morbidity and mortality, as demonstrated by our study's 30% mortality rate, which aligns with prior research¹¹. The primary cause of death was infection, likely due to the heightened risk associated with prolonged ICU and hospital stays, highlighting the critical need for strict infection control measures to reduce mortality. Among the survivors, all experienced long-term sequelae, including epilepsy, memory impairment, and psychiatric or behavioral issues. Notably, epilepsy was observed in 100% of the survivors, who received continuous treatment with anti-seizure medications.

In addition to the high mortality rate, the morbidity burden in NORSE is substantial, as reflected by the median modified Rankin Scale (mRS) score of 4 at six months, indicating moderate to severe disability. This finding is consistent with the poor long-term outcomes reported in earlier studies¹¹. However, there is some optimism: functional outcomes showed a trend of continuous improvement over time, with the median mRS improving to 3 at 12 months and the median mRS 2 at the latest follow-up. This underscores the potential for long-term recovery in survivors, albeit with significant residual challenges.

Strengths and Limitations

This study benefits from comprehensive data collection across a wide range of clinical variables and an extended follow-up period, offering valuable insights into the long-term prognosis of patients with cryptogenic NORSE. As one of the first studies on cryptogenic NORSE conducted in Thailand, it pro-

vides novel and region-specific findings that contribute to the existing body of knowledge. Nevertheless, certain limitations should be acknowledged. The relatively small sample size (n=20) restricts the generalizability of the results, underscoring the need for larger, multicenter studies to confirm these findings. Additionally, the retrospective study design may introduce potential biases, such as incomplete or missing data. Moreover, reliance on the modified Rankin Scale (mRS) as a primary outcome measure may not fully capture the breadth of neurological and cognitive impairments experienced by survivors, highlighting the need for more comprehensive and multidimensional assessment tools in future research.

Conclusion

Cryptogenic NORSE is associated with high morbidity and mortality. However, approximately 50% of patients may achieve a favorable functional outcome. Factors associated with poor prognosis include lower CSF white blood cell counts and a higher number of anesthetic agents used.

Acknowledgement

This work was financially supported by Grant No.66022 from the Neurological Institute of Thailand, Department of Medical Services, Ministry of Public Health, Thailand.

References

1. Gaspard N, Hirsch LJ, Sculier C, Loddenkemper T, van Baalen A, Lancrenon J, et al. New-onset refractory status epilepticus (NORSE) and febrile infection-related epilepsy syndrome (FIRES): State of the art and perspectives. *Epilepsia* 2018;59:745-52.
2. Werbaneth K, Mausolf M, Seliger J, Le S. A retrospective cohort study of new-onset refractory status epilepticus

- (NORSE): Clinical features, timing of immunotherapy and outcomes. *Epileptic Disorders* 2022;24:867-76.
3. Serino D, Santarone ME, Caputo D, Fusco L. Febrile infection-related epilepsy syndrome (FIRES): Prevalence, impact and management strategies. *Neuropsychiatr Dis Treat* 2019;15:1897-903.
 4. Gaspard N. A New Hose to extinguish the FIRES? *Epilepsy Currents* 2019;19:86-7.
 5. van Baalen A, Vezzani A, Häusler M, Kluger G. Febrile infection-related epilepsy syndrome: Clinical review and hypotheses of epileptogenesis. *Neuropediatrics* 2017;48:5-18.
 6. Tan TH-L, Perucca P, O'Brien TJ, Kwan P, Monif M. Inflammation, ictogenesis, and epileptogenesis: An exploration through human disease. *Epilepsia* 2021; 62:303-24.
 7. Sculier C, Gaspard N. New onset refractory status epilepticus (NORSE). *Seizure* 2019;68:72-8.
 8. Donnelly JP, Kasatwar N, Hafeez S, Seifi A, Gilbert A, Barthol C, et al. Resolution of cryptogenic new onset refractory status epilepticus with tocilizumab. *Epilepsy & Behavior Reports* 2021;15:100431.
 9. Jun J-S, Lee S-T, Kim R, Chu K, Lee SK. Tocilizumab treatment for new onset refractory status epilepticus. *Annals of Neurology* 2018;84:940-5.
 10. Specchio N, Pietrafusa N. New-onset refractory status epilepticus and febrile infection-related epilepsy syndrome. *Developmental Medicine & Child Neurology* 2020;62:897-905.
 11. Gaspard N, Foreman BP, Alvarez V, Cabrera Kang C, Probasco JC, Jongeling AC, et al. New-onset refractory status epilepticus. *Neurology* 2015;85:1604-13.
 12. Jose J, Keni RR, Hassan H, Menon R, Sukumaran S, Cherian A, et al. Predictors of outcome in super refractory status epilepticus. *Epilepsy & Behavior* 2021; 118:107929.
 13. Jayalakshmi S, Vooturi S, Sahu S, Yada PK, Mohandas S. Causes and outcomes of new onset status epilepticus and predictors of refractoriness to therapy. *Journal of Clinical Neuroscience* 2016;26:89-94.
 14. Saitoh M, Kobayashi K, Ohmori I, Tanaka Y, Tanaka K, Inoue T, et al. Cytokine-related and sodium channel polymorphism as candidate predisposing factors for childhood encephalopathy FIRES/AERRPS. *Journal of the Neurological Sciences* 2016;368:272-6.
 15. Wickström R, Taraschenko O, Dilella R, Payne ET, Specchio N, Nabbout R, et al. International consensus recommendations for management of new onset refractory status epilepticus (NORSE) including febrile infection-related epilepsy syndrome (FIRES): Summary and clinical tools. *Epilepsia* 2022;63:2827-39.
 16. Mantoan Ritter L, Nashef L. New-onset refractory status epilepticus (NORSE). *Practical Neurology* 2021; 21:119.
 17. Yanagida A, Kanazawa N, Kaneko J, Kaneko A, Iwase R, Suga H, et al. Clinically based score predicting cryptogenic NORSE at the early stage of status epilepticus. *Neurology Neuroimmunology & Neuroinflammation* 2020; 7:e849.
 18. Rossetti AO, Logroscino G, Milligan TA, Michaelides C, Ruffieux C, Bromfield EB. Status Epilepticus Severity Score (STESS). *Journal of Neurology* 2008;255:1561-6.
 19. Culleton S, Talenti G, Kaliakatsos M, Pujar S, D'Arco F. The spectrum of neuroimaging findings in febrile infection-related epilepsy syndrome (FIRES): A literature review. *Epilepsia* 2019;60:585-92.
 20. Gofton TE, Gaspard N, Hocker SE, Loddenkemper T, Hirsch LJ. New onset refractory status epilepticus research. *Neurology* 2019;92:802-10.
 21. Iizuka T, Kanazawa N, Kaneko J, Tominaga N, Nonoda Y, Hara A, et al. Cryptogenic NORSE. *Neurology Neuroimmunology & Neuroinflammation* 2017;4:e396.
 22. Trinka E, Cock H, Hesdorffer D, Rossetti AO, Scheffer IE, Shinnar S, et al. A definition and classification of status epilepticus – Report of the ILAE Task Force on Classification of Status Epilepticus. *Epilepsia* 2015;56: 1515-23.
 23. Mauritz M, Hirsch LJ, Camfield P, Chin R, Nardone R, Lattanzi S, et al. Acute symptomatic seizures: an educational, evidence-based review. *Epileptic Disorders* 2022;24:26-49.
 24. Pattanaphesaj J, Thavorncharoensap M. The Thai version of the EQ-5D-5l health questionnaire. *Heal Interv Technol Assess Progr* 2015;3:3-6.
 25. Scale S. Modified Rankin Scale. <http://www.strokecenter.org/trials/scales/rankin.html>. 2008.