Epilepsy & Behavior 101 (2019) 106413

Contents lists available at ScienceDirect

Epilepsy & Behavior

journal homepage: www.elsevier.com/locate/yebeh

Incidence of the different stages of status epilepticus in Eastern Finland: A population-based study

Anne-Mari Kantanen [a,*], Joni Sairanen [a], Reetta Kälviäinen [a,b]

[a] Epilepsy Center, Neuro Center, Kuopio University Hospital, Kuopio, Finland
[b] Institute of Clinical Medicine, University of Eastern Finland, Kuopio, Finland

ARTICLE INFO

Article history:
Received 2 June 2019
Accepted 4 July 2019
Available online 29 July 2019

Keywords:
Seizures
Epilepsy
Epidemiology
Refractory
Super-refractory
Definition

ABSTRACT

Objective: The objective of this study was to determine the incidence in Eastern Finland of the different stages of status epilepticus (SE): 1) at the early stage of SE (a prolonged seizure lasting over 5 min);, 2) refractory SE (RSE), and 3) super-refractory SE (SRSE).
Methods: Firstly, we conducted a retrospective study on the incidence and outcome of intensive care unit (ICU)-treated RSE and SRSE in the adult population (≥16 years) in Kuopio University Hospital (KUH)'s special care responsibility area (840,000 inhabitants). Secondly, we conducted a prospective study using the International League Against Epilepsy (ILAE)'s new definition for SE (prolonged seizures lasting over 5 min), in adult (≥16 years) patients in the KUH municipality district (North Savo, 248,000 inhabitants).
Results: The retrospective study on ICU-treated RSE and SRSE from 2010 to 2012 identified 75 patients with RSE, of whom 21% were treated as SRSE, resulting in an annual age-adjusted incidence of ICU-treated RSE of 3.0/100,000 (95% confidence interval [CI]: 2.4–3.8) and 0.6/100,000 (95% CI: 0.4–1.0) for SRSE. In the prospective study of early stage SE (seizures lasting over 5 min), we identified 151 consecutive episodes during the 9-month study period in 2015, corresponding to an annual age-adjusted incidence of 81.1/100,000 (95% CI: 75.8–87.0). In this study, 11 seizure episodes became refractory, resulting in an age-adjusted incidence of RSE of 6.0/100,000 (95% CI: 3.4–10.4), of which seven were treated in the ICU [3.8/100,000 (95% CI: 1.8–7.8)], four were treated palliatively [2.2/100,000 (95% CI: 0.82–5.7)], and two evolved to SRSE [1.1/100,000 (95% CI: 0.3–4.3)].
Conclusions: The new ILAE 2015 definition of SE resulted in a four-fold increase in incidence of SE compared to the earlier 30-min definition reported earlier in Europe. In the epidemiology of RSE, the incidence of ICU-treated RSE, palliatively treated RSE, and SRSE needs to be separated.
This article is part of the Special Issue "Proceedings of the 7th London-Innsbruck Colloquium on Status Epilepticus and Acute Seizures.
© 2019 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

1. Introduction

Status epilepticus (SE) is a neurological emergency with high morbidity and mortality. When seizures of any type persist, they are considered as a separate condition, known as SE [1]. The 2015 International League Against Epilepsy (ILAE) taskforce defined SE as "a condition resulting either from the failure of the mechanisms responsible for seizure termination or from the initiation mechanisms, which lead to abnormally prolonged seizures" [2]. In tonic–clonic seizures, the ILAE taskforce's novel definition of SE is an epileptic activity lasting over 5 min and in focal seizures, an epileptic activity exceeding 10 min [2]. Status epilepticus becomes refractory SE (RSE) if the first- and second-line treatments with benzodiazepines and antiepileptic drugs (AEDs) fail to terminate the seizure activity [3]. Status epilepticus is defined as super-refractory SE (SRSE) if it continues more than 24 h after the first administration of general anesthesia [3].

The definition of SE has evolved through the years, and the timeframe for starting the medication has shortened, even though the fundamental concept of prolonged seizures has remained the same. Status epilepticus incidence varies in different populations and according to the definition used in each study. Studies of population-based incidence are scarce compared to hospital-based cohorts, and exact definitions of the different SE types are seldom used. The incidence of established SE (prolonged seizure lasting over 30 min; definition recommended earlier for epidemiological studies) varies widely in different parts of the world: the lowest reported incidence is in Asia (5.2/100,000) [4], the highest is in the United States 41/100,000 [5–7], and in Europe, it has been reported between 10 and 16/100,000 [8,9]. Population-based studies on the incidence of RSE and SRSE are even rarer. The nationwide population-based incidence for RSE and SRSE in

* Corresponding author at: Epilepsy Center, Neurocenter, Kuopio University Hospital, P.O. Box 100, Kuopio FI 70029, Finland.
E-mail address: anne-mari.kantanen@nly.fimnet.fi (A.-M. Kantanen).

https://doi.org/10.1016/j.yebeh.2019.07.014
1525-5050/© 2019 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Finland has been reported by our study group [10,11]. A recent article by Leitinger et al. [12] was the first epidemiological study to use the 5-min definition of SE, reporting an incidence of 36.1/100,000. Table 1 provides an overview of the published population-based incidence studies.

The present study aimed to determine the incidence of SE, defined as prolonged seizures lasting over 5 min, and of RSE and SRSE in two different population-based studies in Eastern Finland.

2. Material and methods

We combined the data from two studies conducted in Kuopio University Hospital (KUH)'s special care responsibility area during the years 2010–2015 to collect population-based epidemiological data on early SE, RSE, and SRSE and compared the incidence of the different study populations. The study areas are presented in Fig. 1.

2.1. ICU-treated refractory and super-refractory status epilepticus 2010–2012

Firstly, we conducted a retrospective study on the incidence and outcome of intensive care unit (ICU)-treated RSE and SRSE in the adult population (≥16 years) in KUH special care responsibility area hospitals' ICUs in the eastern part of Finland from January 1, 2010 to December 31, 2012. The KUH special care responsibility area consists of five hospitals, one university hospital (KUH) and four central hospitals, covering a population of 840,000 inhabitants (Fig. 1.). We used the Finnish Intensive Care Consortium database to identify the ICU-treated RSE and SRSE during the three-year period and excluded patients with postanoxic etiologies. In the KUH area, the five public hospitals provide all the neuroemergency services and intensive care. The incidence of ICU-treated RSE and SRSE has previously been published as part of a long-term outcome study [20].

2.2. Acute seizures presenting to the neuroemergency department of Kuopio University Hospital

Secondly, we conducted a prospective study of acute seizures and treatment delays using the ILAE new 2015 definition for prolonged seizures lasting over 5 min in adult (≥16 years) patients in KUH municipality district (North Savo, 248,000 inhabitants) [21]. Kuopio University Hospital is a tertiary hospital located in North Savo region, Eastern Finland. It provides the only 24/7 emergency neurologic service to its catchment population. We recruited all consecutive patients with prolonged seizures in the neurologic emergency department of KUH between 23 March and 31 December 2015, by manually going through patient lists. Kuopio University Hospital coordinates the emergency medical system (EMS), and all the nursing homes, healthcare centers, and two small regional hospitals in the area refer their patients with seizure to KUH. The EMS receives annually 340/100,000 calls about seizure-related situations in the KUH area, but not all these seizures are prolonged. The incidence results from this study cohort have not been published previously.

2.3. Ethics

In this registry study, access to medical records was authorized by the individual hospital districts, in accordance with Finnish legislation.

2.4. Statistics

The incidence and the confidence intervals (CI) were counted as the number of episodes divided by the population at risk (adults ≥ 16 years) of an event in one year with a single rate using a single rate incidence calculator.

3. Results

In the 2010–2012 retrospective study, we identified 75 patients with ICU-treated RSE and 16 patients treated as SRSE in a population of 840,000 over the three years, resulting in an annual age-adjusted incidence of 3.0/100,000 (95% CI: 2.4–3.8) for ICU-treated RSE and 0.6/100,000 (95% CI: 0.4–1.0) for SRSE.

In the prospective study of early SE (seizures lasting over 5 min), we identified 151 consecutive prolonged seizure episodes during the 9-month period in a population of 248,000, which corresponds to an annual age-adjusted incidence of 81.1/100,000 (95% CI: 75.8–87.0). These episodes were experienced by 137 patients, giving a population-based age-adjusted incidence for a first SE episode of 73.7/100,000 (95% CI: 67.6–80.3).

In the prospective study, 11 seizure episodes became refractory, resulting in an age-adjusted incidence of RSE 6.0/100,000 (95% CI:

Table 1
Population-based studies on status epilepticus (SE).

SE definition used	Study	Period covered	Geography	Total cases	Incidence per 100,000	Included	Ref.
Early SE (>5 min)							
ILAE 2015	Leitinger et al., 2019	2011–2015	Salzburg, Austria	221	36.1	Adults (≥18)	[12]
ILAE 2015[a]	Nazerian et al., 2019	2016	Florence, Italy	101	16	Adults (≥18)	[13]
Established SE (>30 min)	DeLorenzo et al., 1996	1989–1991	Richmond, VA, US	166	41	Children and adults	[5]
	Hesdorffer et al., 1998	1965–1984	Rochester, MN, US	199	18.3	Children and adults	[6]
	Coeytaux et al., 2000	1997–1998	French-speaking Switzerland	172	10.3	Children and adults	[9]
	Knake et al., 2001	1997–1999	Marburg, Germany	150	17.1	Adults	[8]
	Wu et al., 2002	1991–1998	California, US	15,601	6.2	Children and adults	[14]
	Vignatelli et al., 2003	1999–2000	Bologna, Italy	44	10.7	Adults	[15]
	Chin et al., 2006	2002–2004	London, UK	226	14.5	Children	[16]
	Timkao et al., 2015	2004–2012	Thailand	12,367	1.3–5.2	SE	[4]
	Bhalla et al., 2014	2004–2005	Reunion, France	65	8.5	Children and adults	[17]
	Schubert-Bast et al., 2019	2008–2015	Germany (insurance data)	282	17.6	Children (0–18)	[18]
Refractory status epilepticus	Leitinger et al., 2019	2011–2015	Salzburg, Austria	221	7.2	Adults (≥18)	[12]
	Schubert-Bast et al., 2019	2008–2015	Germany (insurance data)	282	3.9	Children (0–18)	[18]
	Hesdorffer et al., 1998[b]	1965–1984	Rochester, MN, US	199	7.2	Children and adults	[6]
	Kantanen et al., 2017	2010–2012	Finland	395	3.4	Adults (≥16), ICU	[11]
	Abbasi & Leach, 2019	2013–2016	Glasgow, Scotland	633	20	Adults (>16), ICU	[19]
Super-refractory status epilepticus	Leitinger et al., 2019	2011–2015	Salzburg, Austria	221	1.2	Adults (≥18)	[12]
	Schubert-Bast et al., 2019	2008–2015	Germany (insurance data)	282	2.3	Children (0–18)	[18]
	Hesdorffer et al., 1998[b]	1965–1984	Rochester, MN, US	199	4.6	Children (0–18)	[6]
	Kantanen et al., 2015	2010–2012	Finland, ICU data	395	0.7	Adult (≥16)	[10]

[a] ILAE 2015 definition, exact timepoints not mentioned.
[b] Estimated from the population-based analysis afterwards.

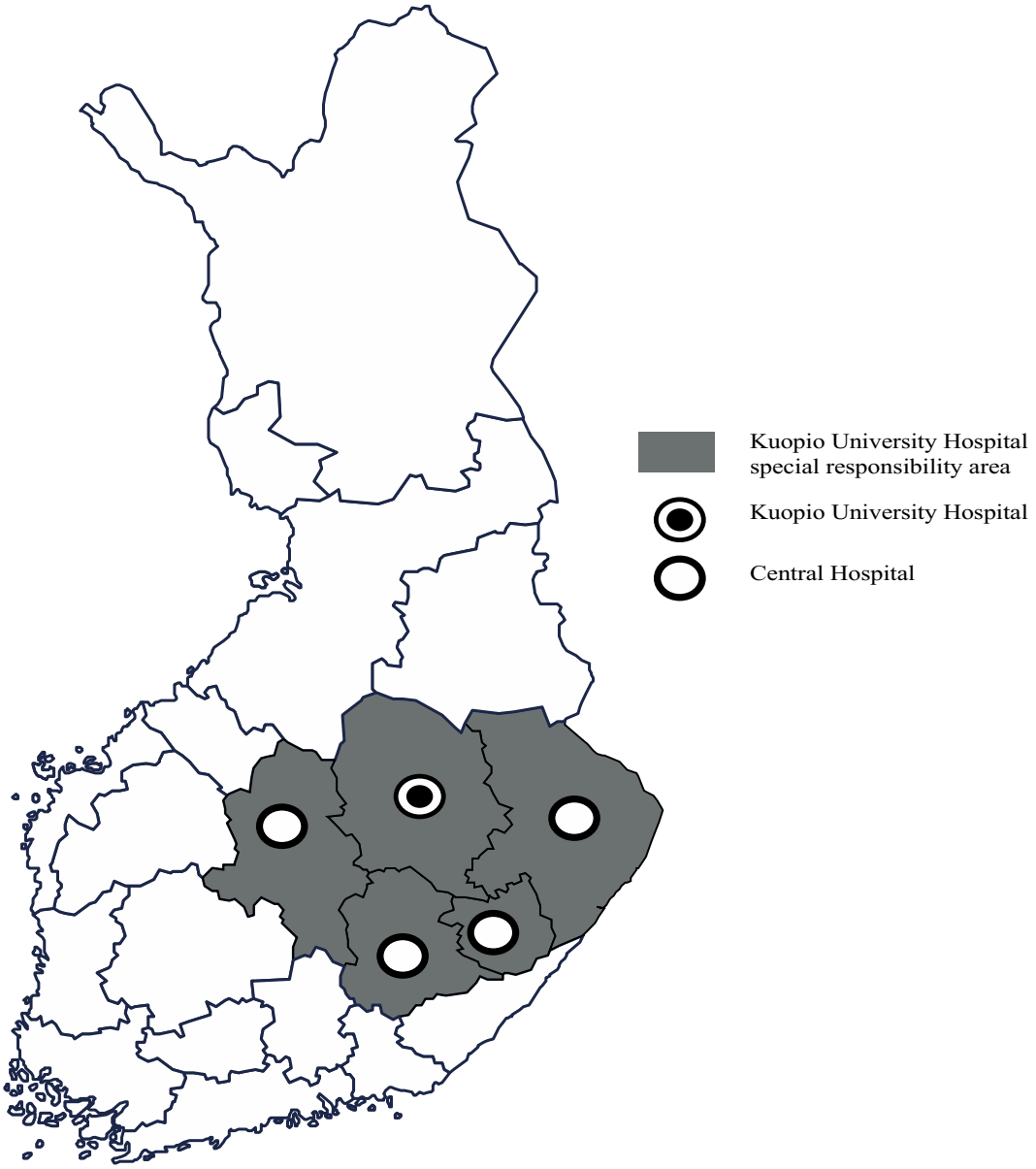

Fig. 1. Kuopio University Hospital special responsibility area (gray) and all the 5 hospital districts including the Kuopio University Hospital municipality district (North Savo).

3.4–10.4). Seven of these patients were treated at the ICU with general anesthesia, leading to the age-adjusted incidence of ICU-treated RSE of 3.8/100,000 (95% CI: 1.8–7.8). Two of the patients further evolved to SRSE; age-adjusted incidence 1.1/100,000 (95% CI: 0.3–4.3). Four of the patients with RSE had limited life expectancy; their ICU treatment was considered futile, and they were instead treated palliatively, giving an age-adjusted incidence of 2.2/100,000 (95% CI: 0.82–5.7).

The most common seizure type in the prospective study was tonic–clonic seizure (105 episodes and an annual incidence of 56.5/100,000 (95% CI: 49.8–64.0)). Acute symptomatic seizures were the most common etiology of SE, with 57 episodes resulting in an annual incidence of 30.6/100,000 (24.7–38.0). Alcohol withdrawal was the most common acute etiology (N = 26) 14.0/100,000 (95% CI: 9.8–20.0), followed by previous cerebrovascular insult (N = 24) and preexisting epilepsy disorder (N = 24) as most common remote symptomatic etiologies. The incidences of different seizure types and etiologies are summarized in Table 2. The overall mortality in this study was 9.0% (12/133) after one-month follow-up. Eight patients died after successful seizure

Table 2
Incidences of status epilepticus (over 5 min) per 100,000 by seizure type and etiology.

Seizure type (N)	Incidence (95% CI)	Etiology (N)	Incidence (95% CI)
Tonic–clonic (105)	56.5 (49.8–64.0)	Acute symptomatic (57)	30.6 (24.7–38.0)
Focal impaired awareness (22)	11.8 (8.0–17.5)	Unknown (15)	8.1 (5.0–13.1)
Nonconvulsive comatose (5)	2.7 (1.1–6.4)	Remote symptomatic (62)	33.3 (27.2–40.8)
Focal aware (15)	8.0 (5.0–13.1)	Progressive symptomatic (17)	9.1 (5.8–14.4)
Absence (2)	1.1 (0.3–4.3)		
Myoclonic (2)	1.1 (0.3–4.3)		

CI (confidence interval).

cessation with first- and second-line AEDs, because of underlying etiological diseases; and four patients with RSE and palliative treatment for SE died. Mortality in the ICU-treated patients was 0%.

4. Discussion

These two studies show the incidence of different stages of SE from early SE to RSE and SRSE in a European population (mainly white Caucasian). The conceptual progress in the definition of SE during recent years is prone to alter the SE incidence and improve its recognition in the early stage instead of the later established stage (seizure activity lasting over 30 min). Detailed epidemiological data are also mandatory for better management and resource allocation for the refractory stages of SE.

In this cohort, the average cumulative incidence of all SE seizure types, according to the ILAE 2015 definition (>5 min), was 81/100,000, which is four-fold higher than that reported in earlier studies from around the world with a 30-min definition of SE (Table 1). Compared to the most recent publication from Europe with the same ILAE definition, from the Salzburg city area, Austria [12], the incidence in this study for a first SE episode was two-fold higher (74/100,000 compared with 36/100,000).

Studies of population-based SE incidence are scarce, and it is possible that studies miss some of the episodes of each entity. In this study, the healthcare system in Finland, the public hospital network, and the emergency services centralization for critically ill patients gave the opportunity to obtain population-based data, especially as only one hospital provides 24/7 neuroemergency services in our municipality district. Patients in the study cohort were referred from their homes and public places, nursing homes, primary healthcare wards, and small regional hospitals [21]; only patients receiving hospice care who were not being actively treated and were not referred to hospital care were omitted from the cohort. According to the Finnish National Institute for Health and Welfare, the KUH hospital district's age-standardized general morbidity index in 2015 was 131.2, the highest in the country (the index for the entire nation being defined as 100) [22]. Differences in overall morbidity and practices in referring severely ill patients to hospital care due to SE might thus explain differences in the SE incidence between North Savo and Salzburg. The Salzburg group recognized a possible underestimation of the incidence because of missing the most seriously ill patients who were not referred [12].

Incidence is also affected by the age distribution, the underlying etiologies, and the comorbid diseases [5,6,9,12,15,23]. In the study cohort, the median age was lower [21] than in the Salzburg population [12]; inclusion of more elderly patients does not explain the difference, however. One possible explanation could be differences in the underlying etiologies. Alcohol consumption in this study's municipality area is higher than the national average [24]. Alcohol withdrawal was the single most common acute symptomatic etiology in this study (14%), and might be reflected in the higher incidence of SE in our area. A similar phenomenon has been reported in the Glasgow area of Scotland [20].

The RSE incidence was 6.0/100,000 in our study and 8.4/100,000 (RSE + SRSE) in the Salzburg study. The Salzburg group used stricter criteria for RSE: they defined RSE when therapy with one first-line benzodiazepine and one second-line AED failed. In our prospective cohort, we used a slightly wider, pragmatic definition of RSE, namely if the patients had failed their first- and second-line AEDs. In our area, any EMS ambulance unit can start treatment with buccal midazolam; advanced life support units can administer intravenous benzodiazepines; and emergency physicians in the field can administer second-line treatments. Therefore, in the hospital, the patients are usually again given more second-line AEDs, and the response is then further evaluated. In practice, it is hard to differentiate the patient's response after only one benzodiazepine and one second-line AED. This is reflected in the Salzburg study, where the majority of patients defined as RSE continued to receive second-line AEDs (41/53); only 4/53 were patients with ICU-treated RSE and 8/53 were patients with SRSE. In our series, we defined patients with RSE either as treated at the ICU with third-line therapy or as palliative care patients with RSE. We speculate that among those 41 patients in the Salzburg, some could be seen as responsive to second-line AEDs and some could be seen as palliative patients with RSE; with this classification, the incidence would be similar to that in this study.

The incidence of ICU-treated RSE (3.8/100,000) and SRSE (1.1/100,000) in the prospective study in the KUH area was somewhat higher than in the retrospective study (RSE: 3.0/100,000 and SRSE: 0.6/100,000). The SRSE incidence was similar to the SRSE incidence of the Salzburg study (1.2/100,000). The ICU-treated RSE incidence in the Salzburg study seems quite low (1.8/100,000). In this study, the incidence for patients whose seizures were refractory but not treated at the ICU for their RSE was 2.2/100,000. These patients were treated with first- and second-line AEDs intravenously and with palliative care instead of general anesthesia in the ICU, based on their comorbidities, prior morbidity, and frailty, presuming futility of treatment in the ICU. There is a growing demand for well-planned and individually tailored management of acute seizures and SE for patients already in palliative care. To prevent unnecessary hospitalization, reduction of quality of life and discomfort to patients, advance care planning, including seizure management, should be done early in the course of the disease. Unlimited and aggressive ICU treatment of RSE in palliative patients is mostly not indicated and can be futile and harmful [25]. Future epidemiological studies of RSE should separate actively the ICU-treated patients and palliatively-treated patients.

The overall mortality in our prospective study was 9% after one-month follow-up. The ICU mortality was 0%. Eight of the patients died because of their comorbidities and etiological diseases, despite the SE being controlled with first-and second-line AEDs. This indicates that the population treated in our hospital also includes very seriously ill patients. Status epilepticus mortality is heavily influenced by the underlying etiology, but the hope is that with more accurate definitions and with staged therapy, the outcomes can change. A recent meta-analysis of the mortality of convulsive SE, however, shows that there is no evidence of better survival over time, and more carefully defined epidemiological studies of different stages and types of SE are desperately needed to better design treatment [26].

The limitations of this study include the relatively small cohort size. Our cohorts do not include those patients with SE who were not treated in KUH emergency department or in the other four hospitals because of special circumstances, for example, do-not-hospitalize orders. The general morbidity and our local EMS guidelines have influenced the results, and therefore, our results may not be readily generalized to other populations with different morbidity, genetics, and access to care even in Finland.

5. Conclusion

The population-based incidence using the new ILAE 2015 definition is considerably higher than previously, up to 81/100,000 of SE, whereas the incidence of RSE and SRSE remains at a relatively low level. This study and the other recent population-based studies of SE incidence enable an estimate of the population-based incidence of the different stages of SE, as presented in Fig. 2. Changing the definition towards early recognition and treatment makes SE more noticeable in the healthcare system and provides more awareness of this severe neurological emergency with substantial mortality and morbidity. New epidemiological data on SE are needed, and the definitions for different stages of SE should be used in the studies to make them more comparable. In the epidemiology of RSE, the incidence of ICU-treated RSE, palliatively-treated RSE, and SRSE needs to be separated.

Declaration of Competing Interest

AMK has received a grant from the Finnish Cultural Foundation and speaker's honoraria from Orion, Boehringer Ingelheim, MSD, BMS and a

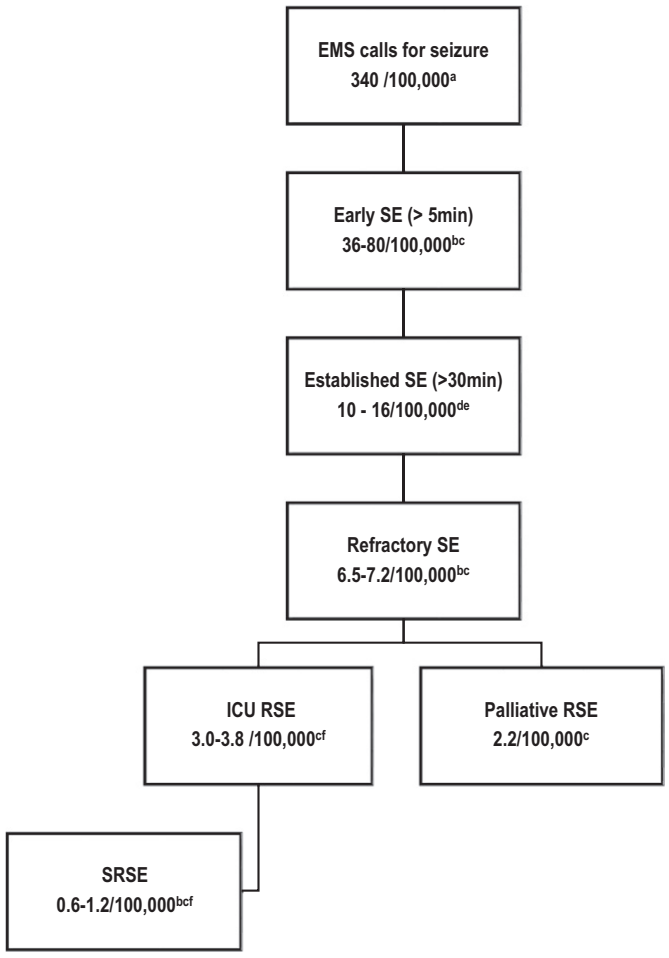

Fig. 2. Incidences of different stages of status epilepticus (SE). EMS = emergency medical services; ICU = intensive care unit; RSE = refractory status epilepticus; SRSE = super-refractory status epilepticus. ([a]Kälviäinen et al. [27], [b]Leitinger et al. [12], [c]current study, [d]Knake et al. [8], [e]Coeytaux et al. [9], [f]Kantanen et al. [20]).

travel grant from Sanofi. JS has received grants from the Finnish Epilepsy Research Foundation and the Maire Taponen Foundation and institutional funding from the Saastamoinen Foundation through the University of Eastern Finland Clinical Epileptology Group Grant. RK has received institutional grants from the Academy of Finland and the Saastamoinen Foundation; speaker's honoraria from Eisai, Orion, Sandoz, and UCB; and honoraria for the membership of advisory boards from Eisai, GW Pharmaceuticals, Marinus Pharmaceuticals, Takeda, and UCB.

Acknowledgment

Kuopio University Hospital Government Funding (VTR), Finnish Epilepsy Research Foundation, Finnish Cultural Foundation and Saasatamoinen Foundation and Maire Taponen Foundation.

References

[1] Shorvon S. Status epilepticus: its clinical features and treatment in children and adults. Cambridge: Cambridge University Press; 1994.
[2] 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.
[3] Shorvon S, Ferlisi M. The outcome of therapies in refractory and super-refractory convulsive status epilepticus and recommendations for therapy. Brain 2012;135:2314–28.
[4] Timkao S, Pranboon S, Thepsuthammarat K, Sawanyawisuth K. Incidences and outcomes of status epilepticus: a 9-year longitudinal study. Epilepsy Behav 2015;49:135–7.
[5] DeLorenzo RJ, Hauser WA, Towne AR, Boggs JG, Pellock JM, Penberthy L, et al. A prospective, population based epidemiologic study of status epilepticus in Richmond, Virginia. Neurology 1996;46:1029–35.
[6] Hesdorffer DC, Logroscino G, Cascino G, Annegers JF, Hauser WA. Incidence of status epilepticus in Rochester Minnesota, 1965–1984. Neurology 1998;50:735–41.
[7] Dham BS, Hunter K, Ricon F. The epidemiology of status epilepticus in the United States. Neurocrit Care 2014;20:476–83.
[8] Knake S, Rosenow F, Vescovi M, Oertel WH, Mueller HH, Wirbatz A, et al. Incidence of status epilepticus in adults in Germany: a prospective population-based study. Epilepsia 2001;42:714–8.
[9] Coeytaux A, Jallon P, Galobardes B, Morabia A. Incidence of status epilepticus in French- speaking Switzerland: (EPISTAR). Neurology 2000;55:693–7.
[10] Kantanen AM, Kälviäinen R, Parviainen I, Ruokonen E, Ala-Peijari M, Bäcklund T, et al. Incidence and mortality of super-refractory status epilepticus in adults. Epilepsy Behav 2015;49:131–4.
[11] Kantanen AM, Kälviäinen R, Parviainen I, Ala-Peijari M, Bäcklund T, Koskenkari J, et al. Predictors of hospital and one year mortality in intensive care patients with refractory status epilepticus: a population based study. Crit Care 2017;21(1):71.
[12] Leitinger M, Trinka E, Giovannini G, Zimmermann G, Florea C, Rohracher A, et al. Epidemiology of status epilepticus in adults; population based study on incidence, causes and outcomes. Epilepsia 2019;60:53–62.
[13] Nazerian P, Lazzeretti S, Vanni S, Donnarumma E, Magazzini S, Ruggiano G, et al. Incidence, management and short-term prognosis of status epilepticus in the emergency department: population survey. Eur J Emerg Med 2019;26:228–30.
[14] Wu YW, Shek DW, Garcia PA, Zhao S, Johnston SC. Incidence and mortality of generalized convulsive status epilepticus in California. Neurology 2002;58:1070–6.
[15] Vignatelli L, Tonon C, D'Alessandro R, Bologna Group for the Study of Status Epilepticus. Incidence and short-term prognosis of status epilepticus in adults in Bologna, Italy. Epilepsia 2003;44:964–8.
[16] Chin RF, Neville BG, Peckham C, Bedford H, Wade A, Scott RC, et al. Incidence, cause, and short-term outcome of convulsive status epilepticus in childhood: prospective population-based study. Lancet 2006;368(9531):222–9.
[17] Bhalla D, Tchalla AE, Mignard C, Marin B, Mignard D, Jallon P, et al. First ever population-based study on status epilepticus in French Island La Reunion (France)- incidence and fatality. Seizure 2014;23:769–73.
[18] Schubert-Bast S, Zöllner JP, Ansorge S, Hapfelmeier J, Bonthapally V, Eldar-Lissai A, et al. Burden and epidemiology of status epilepticus in infants, children, and adolescents: a population based study on German Health insurance data. Epilepsia 2019;60(5):911–20.
[19] Abbasi H, Leach JP. Refractory status epilepticus in adults admitted to ITU in Glasgow 1995–2013 a longitudinal audit highlighting the need for action for provoked and unprovoked status epilepticus. Seizure 2019;65:138–43.
[20] Kantanen AM, Reinikainen M, Parviainen I, Kälviäinen R. Long-term outcome of refractory status epilepticus in adults: a retrospective population based study. Epilepsy Res 2017;133:13–21.
[21] Sairanen JJ, Kantanen AM, Hyppölä HT, Kälviäinen RK. Treatment delay in status epilepticus – more effective pre hospital symptom recognition warranted. Scand J Trauma Resusc Emerg Med 2019;27(1):28.
[22] Welfare Compass: National Institute for Health and Welfare. Age standardised morbidity index. https://www.hyvinvointikompassi.fi/en/web/hyvinvointikompassi/hyvinvointi-profiili/; 2015, Accessed date: 31 May 2019.
[23] Ong CT, Sheu SM, Tsai CF, Wong YS, Chen SC. Age-dependent sex difference of the incidence and mortality of status epilepticus: a twelve-year nationwide population-based cohort study in Taiwan. Plos one 2015;10(3):e0122350.
[24] National Institute for Health and Welfare. Sosiaali – ja terveyspalvelut Pohjois-Savo. http://www.julkari.fi/bitstream/handle/10024/136998/URN_ISBN_978-952-343-179-9.pdf, Accessed date: 31 May 2019.
[25] Kälviäinen R, Reinikainen M. Management of prolonged epileptic seizures and status epilepticus in palliative care patients. Epilepsy Behav 2019. https://doi.org/10.1016/j.yebeh.2019.04.041.
[26] Neligan A, Noyce AJ, Gosavi TD, Shorvon SD, Köhler S, Walker MC. Change in mortality of generalized convulsive status epilepticus in high-income countries over time. A systematic review and meta-analysis. JAMA Neurol 2019. https://doi.org/10.1001/jamaneurol.2019.1268.
[27] Kälviäinen R, Bendel S, Jonsson H, Keränen T, Kurola J, Kuusela AL, et al. Status epilepticus (30.5.2016). Current care guidelines. The working group set up by Finnish Medical Society Duodecim, the Finnish Pediatric Neurology Society and the Finnish Neurological Society. Available online at: www.kaypahoito.fi, Accessed date: 31 May 2019.