Intensive Care Med (2017) 43:1532–1534
DOI 10.1007/s00134-017-4837-6

LETTER

Super-refractory status epilepticus: epidemiology, early predictors, and outcomes

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Dear Editor,

Super-refractory status epilepticus (SRSE) is defined as the persistence or recurrence of seizures 24 h or more after the initiation of general anesthesia for the management of refractory status epilepticus (SE) [1]. The few epidemiological studies of SRSE produced divergent results, perhaps in part because of their retrospective design, differences in patient recruitment, and variability in the definition of SRSE [2–5]. Moreover, little information exists about predictors of progression to SRSE [2, 5]. Here, our objective was to describe the epidemiology and outcomes of SRSE and to identify early predictors of SRSE in critically ill adults. Our local ethics committee (Comité de Protection des Personnes of Paris—Ile de France XI) approved the study (#13004) and waived the requirement for informed consent, in compliance with French legislation on retrospective observational studies.

Adults with convulsive SE admitted to our teaching hospital-affiliated ICU were identified retrospectively by searching the hospital database for code G41 indicating SE in the International Classification of Diseases (10th Revision). In order not to bias analysis because of the implementation of therapeutic hypothermia in patients included in the HYBERNATUS trial, we restricted the inclusion period between 2005 and 2011 [6]. One-year outcomes were determined using the Glasgow outcome scale (GOS) score by a structured phone interview and/or neurologist visit and charts. To identify associations between patient characteristics and progression to SRSE, we built a multivariate logistic regression model.

Figure 1 is the study flow chart. Tables ESM1 and ESM2 report the main patient characteristics, treatment modalities, and investigations to identify the cause of SE in the 160 patients included in the study. Nineteen (40%) patients progressed to SRSE and received various combinations of propofol ($n = 15$, 78.9%), midazolam ($n = 14$, 73.7%), and thiopental ($n = 11$; 57.9%), concomitantly with a median of 3 [3–4] antiepileptic drugs. Adjuvant anticonvulsant therapy was required in four patients (continuous intravenous magnesium, $n = 1$; corticosteroids, $n = 1$; and therapeutic hypothermia, $n = 2$). As shown in ESM3, the main complications associated with SRSE were ICU-acquired neuromyopathy, deep vein thrombosis, catheter-related infection, urinary tract infection, ventilator-associated pneumonia, and iatrogenic injuries (e.g., cardiac arrest, drug rash with eosinophilia, and systemic symptoms syndrome). Median ICU and hospital lengths of stay were 20 days (IQR 16–33) and 32 days (IQR 21–47), respectively. One-year outcomes were as follows: 8 (42%) patients had died, 1 (5%) was in a persistent vegetative state, 3 (16%) had severe disabilities, 4 (21%) had minimal disabilities, and 3 (16%) had a good recovery. Of the 11 survivors, 9 (81.8%) had persistent epilepsy and 8 (72.7%) persistent mental or physical impairments. By multivariate analysis, CNS infection as the cause of SE was the only identified independent predictor of SRSE (odds ratio 5.42; 95% confidence interval 1.25–21.5; $P = 0.02$) (ESM4).

To conclude, progression to SRSE occurred in a substantial proportion of ICU patients with convulsive SE and was associated with higher frequencies of ICU complications and of adverse outcomes in the short and long terms. CNS infection as the etiology of SE was the only identified predictor of progression to SRSE. These results need further evaluation in a large multicenter prospective

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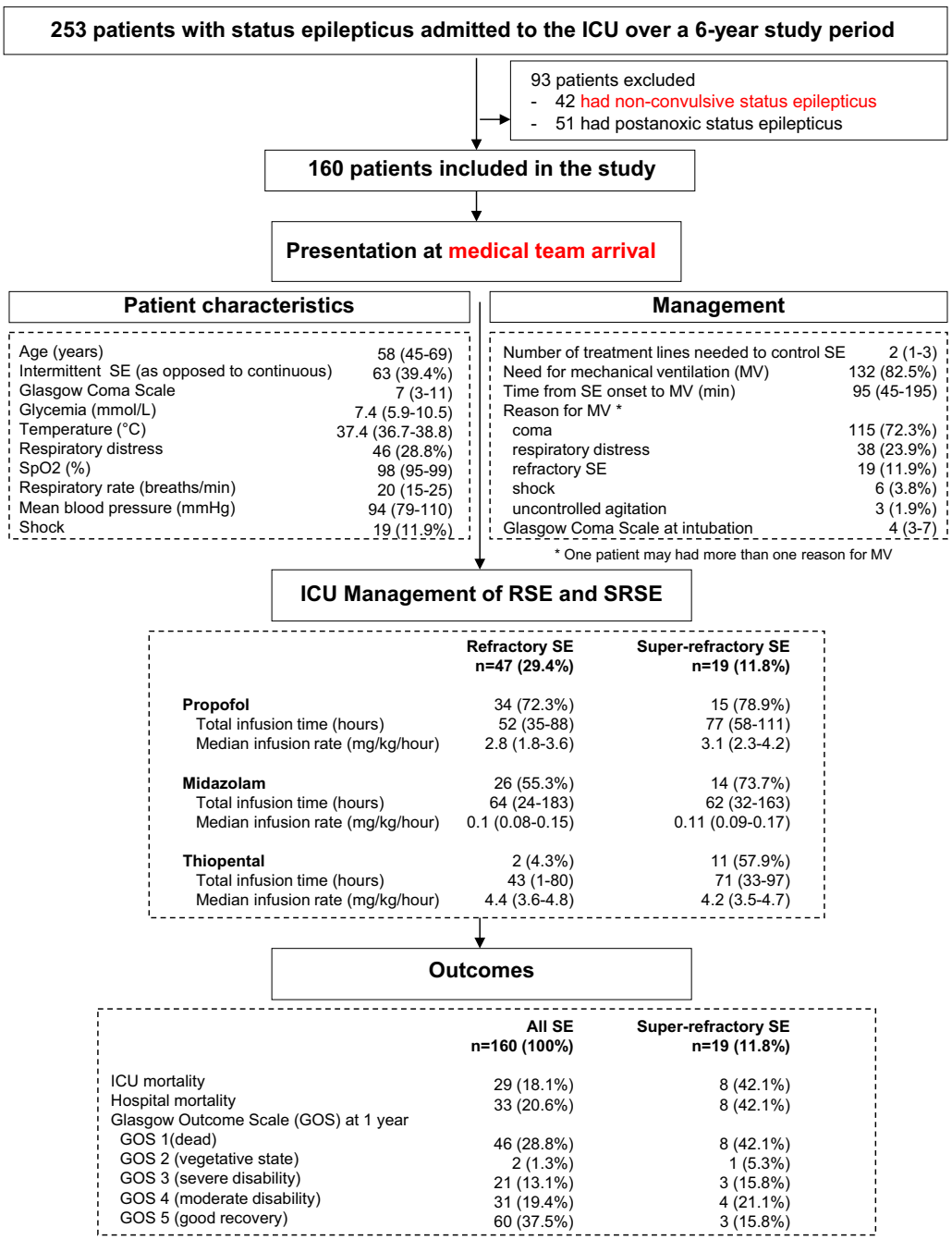

Fig. 1 Patient flow chart, presentation at the scene, management, and 1-year outcomes in 160 patients with convulsive status epilepticus. *ICU* intensive care unit, *SE* status epilepticus, *RSE* refractory status epilepticus, *SRSE* super-refractory status epilepticus, *MV* mechanical ventilation, SpO_2 pulse oximetry, *GOS* Glasgow outcome scale

study. Whether patients admitted to the ICU with CNS infection and SE should receive early aggressive treatment to prevent SRSE may deserve to be investigated.

Electronic supplementary material

The online version of this article (doi:10.1007/s00134-017-4837-6) contains supplementary material, which is available to authorized users.

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Acknowledgements
We thank A. Wolfe MD (Issy-les-Moulineaux, France) for helping to prepare the manuscript. The study was supported by the French public funding agency Délégation à la Recherche Clinique et à l'Innovation (DRCI), Versailles, France.

Compliance with ethical standards

Ethical approval
All procedures involving the patients complied with the ethical standards of the institutional and national research committees and with the 1964 Declaration of Helsinki and its later amendments.

Conflicts of interest
None of the authors has any conflicts of interest to declare.

Accepted: 6 May 2017
Published online: 11 May 2017

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