

Burst-suppression and intravenous anesthetic drugs in patients with refractory status epilepticus in a tertiary medical care center

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Conclusions

1. In adult refractory status epilepticus patients without hypoxic-ischemic encephalopathy treated with intravenous anesthetic drugs, burst-suppression with $\geq 50\%$ suppression proportion was achieved in every fifth patient only.
2. Burst-suppression was not associated with persistent seizure termination, in-hospital survival or return to pre-morbid neurologic function.

Aims of this Study

1. To investigate the frequency of induced EEG burst-suppression pattern (**BS**) during continuous intravenous anesthesia,
2. and associated outcomes in adult patients treated for refractory status epilepticus (**RSE**).

Methods

- RSE patients treated with anesthetics at a Swiss academic care center from 2011-2019 were included (Fig. 2).
- Clinical data and semiquantitative EEG analyses were assessed. BS was categorized as incomplete BS or complete BS (Fig. 1).
- The frequency of induced BS, and association of BS with outcomes (persistent seizure termination, in-hospital survival, and return to pre-morbid neurologic function) were endpoints.

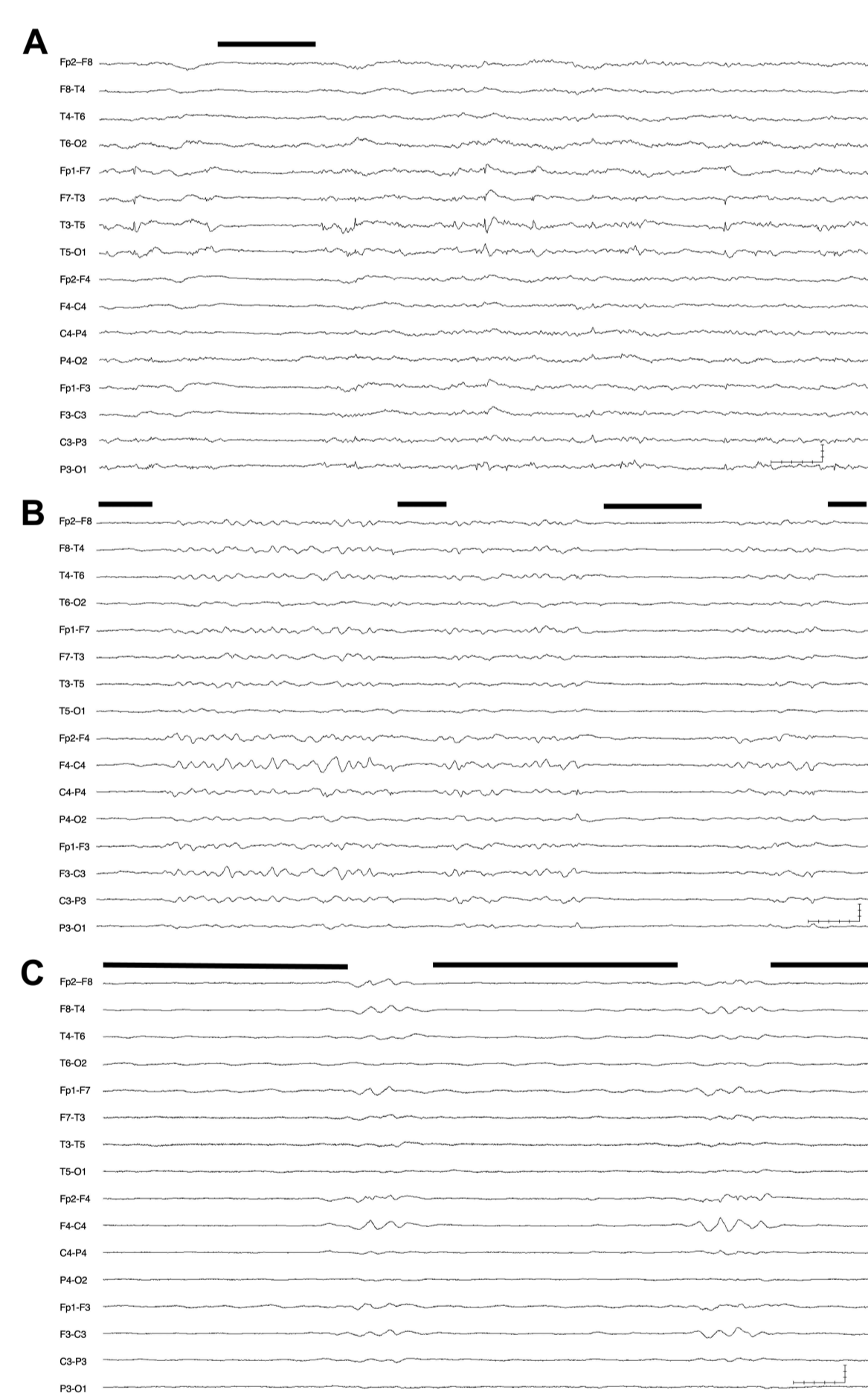


Fig. 1: Semiquantitative analysis of burst-suppression.

- BS was defined according to the current American Clinical Neurophysiology Society's (ACNS) Standardized Critical Care EEG Terminology¹.
- All EEGs during the period of anesthesia were visually analyzed to quantify BS by two trained EEG readers.
- For every hour of EEG recording, the first two-minutes epoch was continuously assessed for segments with suppression/attenuation fulfilling the ACNS criteria that were rounded to whole seconds (bold lines in Fig. 1).
- Three categories were noted:
 - (A) Absence of any burst-suppression pattern ($\leq 20\%$ cumulative suppression/attenuation segments).
 - (B) Incomplete burst-suppression ($\geq 20\%$ and $< 50\%$ suppression/attenuation proportion).
 - (C) Complete burst-suppression ($\geq 50\%$ and $< 100\%$ suppression/attenuation).

All EEGs shown in anterior-posterior bipolar montage using the international 10-20 system for the placement of superficial scalp electrodes, low-pass filter 0.5 Hz, high-pass filter 70 Hz; scale bar: horizontal 1 second, vertical 70 μ V.

Results

A total of 147 patients were included (Fig. 2). Among the 102 patients without hypoxic-ischemic encephalopathy, BS was established in 35 (34.3%) with incomplete BS in 14 (13.7%) and complete BS in 21 (20.5%) (Fig. 3).

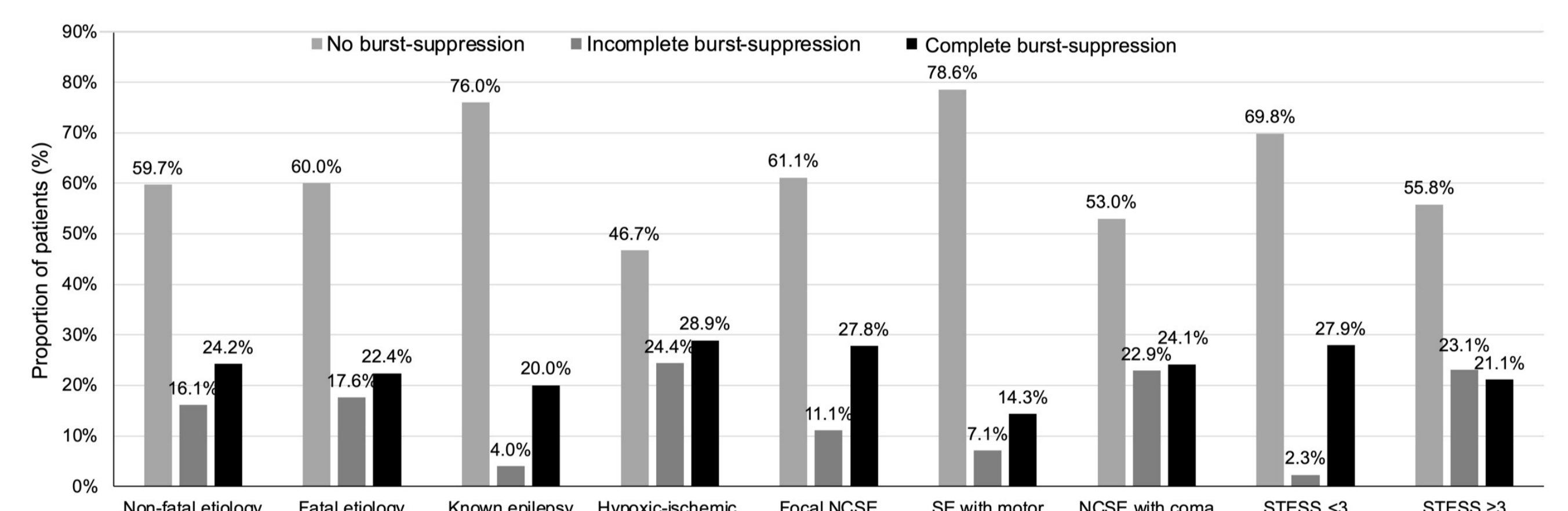
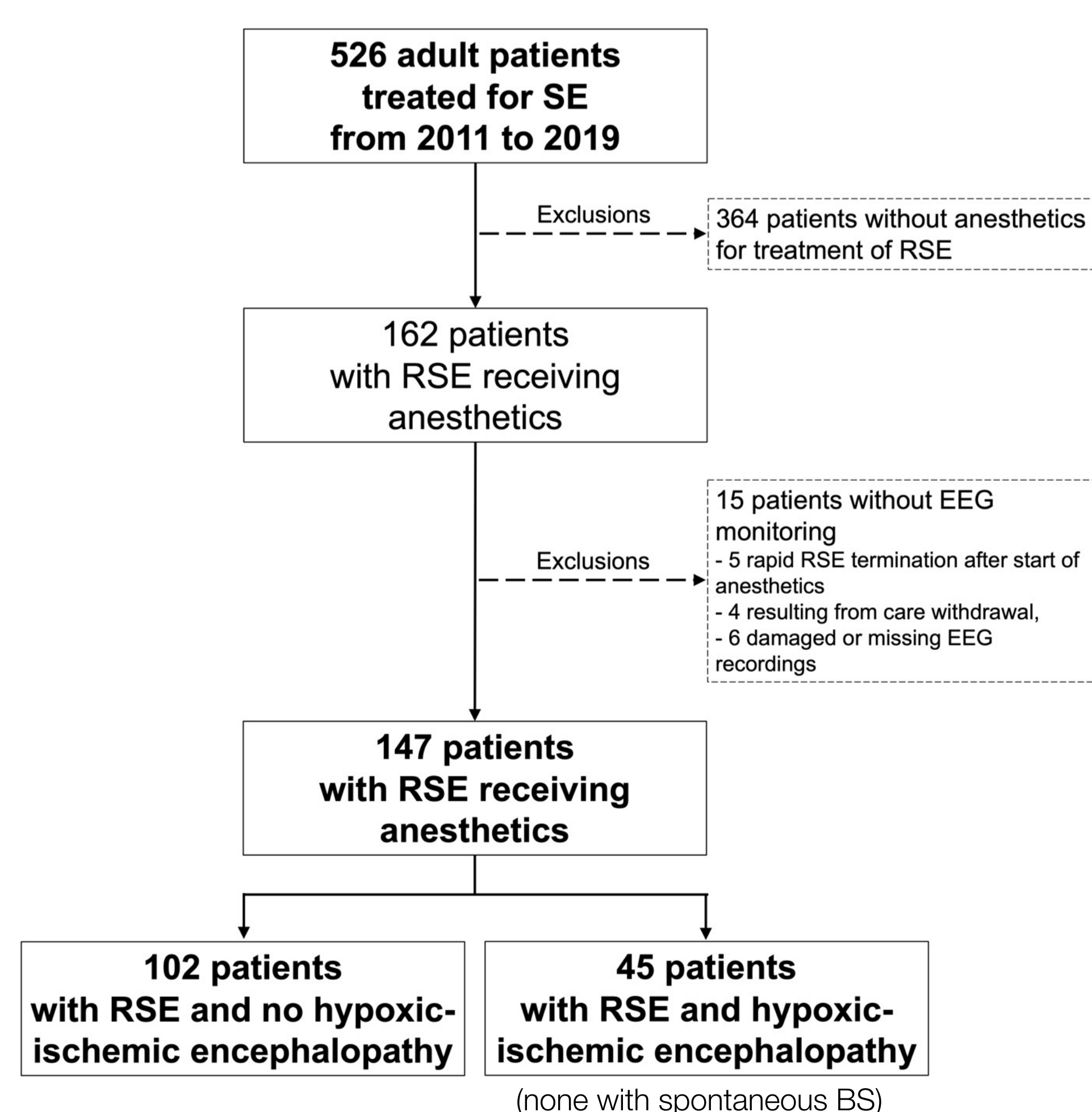


Fig. 3: Proportion of patients with and without complete or incomplete burst-suppression among specific subgroups.

	Odds ratio	95% confidence interval	p-value
Persistent seizure termination			
Any burst-suppression	0.75	0.12-4.72	0.760
Duration of any burst-suppression (increasing hour)	1.01	0.98-1.03	0.614
Complete burst-suppression	1.96	0.12-31.87	0.638
Duration of complete burst-suppression (per increasing hour)	NA	(all patients had persistent seizure termination)	
In-hospital survival			
Any burst-suppression	2.07	0.45-9.45	0.348
Duration of any burst-suppression (increasing hour)	1.01	0.99-1.02	0.634
Complete burst-suppression	4.65	0.44-19.32	0.202
Duration of complete burst-suppression (per increasing hour)	NA	(all patients who died were treated without achieving complete burst-suppression)	
Return to pre-morbid neurologic function in survivors			
Any burst-suppression	0.38	0.12-1.22	0.104
Duration of any burst-suppression (increasing hour)	0.99	0.94-1.01	0.197
Complete burst-suppression	0.72	0.18-2.79	0.630
Duration of complete burst-suppression (per increasing hour)	0.98	0.93-1.02	0.277

Table 1: Multivariable logistic regression analyses regarding the associations between burst-suppression and outcomes in RSE patients without hypoxic-ischemic encephalopathy. Adjusted for potential confounders (identified from univariable comparisons between patients without hypoxic-ischemic encephalopathy with or without induced burst-suppression): Age, Charlson comorbidity Index, STESS, SE with motor symptoms, arterial hypotension requiring vasopressors.

Fig. 2: Flow chart of included and excluded patients.



Background and Discussion

- There is little evidence for BS as an adequate surrogate target for anesthesia titration in RSE patients, which is limited by methodological issues as acknowledged by international guidelines^{2,3}. A current definition of BS specifies a suppression/attenuation proportion of $\geq 50\%$ of the recording¹. However, data supporting the adequacy of this threshold are lacking. Based on this current definition, we semi-quantified BS in EEGs of RSE patients and explored associations with relevant outcomes.
- We report that BS was achieved in up to a third of RSE patients in whom deep anesthesia reflected by BS or persistent seizure suppression was targeted. BS fulfilled the current ACNS criteria in only every fifth patient. These findings are reflected by previous studies which demonstrated the difficulties to establish and maintain a continuous BS⁴.
- Our secondary findings showed that while BS was associated with prolonged mechanical ventilation, severe arterial hypotension requiring the administration of vasopressors, prolonged ICU and hospital stay (data not shown), the achievement and duration of BS was not associated with persistent seizure termination, in-hospital survival, and return to pre-morbid neurologic function after adjusting for potential confounders. Not achieving BS was not associated with adverse outcomes.
- Further and larger studies are needed to validate our findings in adult patients with RSE and to explore if certain subgroups benefit from BS in comparison to seizure cessation as the titration goal for anesthesia.

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Abbreviations:
 ACNS = American Clinical Neurophysiology Society; BS = Burst-suppression; EEG = electroencephalography; NCSE = nonconvulsive status epilepticus; RSE = refractory status epilepticus; SE = status epilepticus; STESS = Status Epilepticus Severity Score.

The authors declare no conflict of interest. Contact: urs.fisch@usb.ch