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### LETTER



# Epilepsia™

# Letter to the editor regarding "early timing of anesthesia in status epilepticus is associated with complete recovery: A 7-year retrospective two-center study"

We read with great interest the recently published paper "Early timing of anesthesia in status epilepticus is associated with complete recovery: A 7-year retrospective two-center study".<sup>1</sup> The authors, focusing on a relevant question, analyzed 246 status epilepticus (SE) episodes receiving intubation (of 762 patients overall with SE treated in two hospitals), concluding that early anesthesia is associated with better outcome, shorter SE duration, and fewer infections.

This article is credited for stimulating the discussion on early SE management. However, these findings have a potential practical impact, as it may be inferred that earlier use of anesthetic drugs than currently recommended<sup>2–4</sup> should be broadly encouraged in patients with SE. However, post hoc analysis of meticulously controlled data from prospective randomized studies showed that both early and late anesthetic treatments are associated with worse clinical outcomes.<sup>5</sup> In addition, decisions to perform endotracheal intubation in established SE is mostly based on local practices, and do not depend entirely on patient characteristics or early clinical recovery after SE treatment.<sup>6</sup> In the present study, the results favoring early intubation may be the consequence of the methods chosen for comparisons.

There is a marked local practice variation across the two centers (e.g., 44% vs 12% of anesthetized patients; in the first center, anesthetics administration occurred as first or second line in >50% of patients); this suggests a natural experiment, and the authors performed statistical adjustment for center of recruitment. However, to avoid information bias (which is statistically not correctable), case ascertainment should be symmetrical across centers; this may be questionable in the studied cohort, as to our knowledge only one center maintains a prospective SE registry since several years.<sup>7</sup>

Furthermore, the authors compared patients who received anesthesia earlier than recommended (as first- or second-line treatment) with those receiving it later (after third-line treatment), but not with those not anesthetized. We fear that this choice may introduce a selection bias (also not amendable with statistics). It has been shown that a consistent proportion of SE patients receiving early anesthesia are intubated post-ictally after a single seizure, or due to nonepileptic events, or in cases of early responding SE,<sup>8</sup> which would have probably responded to any first-line treatment. The surprisingly lower mortality rate of anesthetized patients in the present study (6%), compared to a contemporary multicenter cohort of refractory SE patients receiving anesthesia (27%),<sup>9</sup> supports this hypothesis. Comparing such patients with those experiencing refractory SE (or receiving anesthesia as third or later treatment) does not seem entirely sound. Patients with refractory SE have indeed clearly worse outcomes,<sup>10</sup> and it would have been crucial to at least account for SE refractoriness in the statistical corrections, and to report the proportion of patients dying with ongoing SE.

In summary, it may be possible that SE patients deserve early anesthesia, but before changing current treatment guidelines (which are still insufficiently followed, particularly at the beginning of the SE episode),<sup>11</sup> a proper analysis of the existent data and ideally a randomizedcontrolled trial seem necessary.

### CONFLICT OF INTEREST STATEMENT

None of the authors has any conflict of interest to disclose.

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## REFERENCES

- De Stefano P, Baumann SM, Grzonka P, Sarbu OE, De Marchis GM, Hunziker S, et al. Early timing of anesthesia in status epilepticus is associated with complete recovery: a 7-year retrospective two-center study. Epilepsia. 2023;64:1493–506. https:// doi.org/10.1111/epi.17614
- Brophy GM, Bell R, Claassen J, Bleck TP, Glauser T, Laroche SM, et al. Guidelines for the evaluation and Management of Status Epilepticus. Neurocrit Care. 2012;17:3–23.
- Glauser T, Shinnar S, Gloss D, Alldredge B, Arya R, Bainbridge J, et al. Evidence-based guideline: treatment of convulsive status epilepticus in children and adults: report of the guideline Committee of the American Epilepsy Society. Epilepsy Curr. 2016;16:48–61.
- Outin H, Gueye P, Alvarez V, Auvin S, Clair B, Convers P, et al. Recommandations Formalisées d'Experts SRLF/SFMU: Prise en charge des états de mal épileptiques en préhospitalier, en

structure d'urgence et en réanimation dans les 48 premières heures (A l'exclusion du nouveau-né et du nourrisson). Ann. Fr. Med. Urgence Srlf-Sfmu. 2020;10:151–86.

- Vohra TT, Miller JB, Nicholas KS, Varelas PN, Harsh DM, Durkalski V, et al. Endotracheal intubation in patients treated for prehospital status epilepticus. Neurocrit Care. 2015;23:33–43.
- Rosenthal ES, Elm JJ, Ingles J, Rogers AJ, Terndrup TE, Holsti M, et al. Early neurologic recovery, practice pattern variation, and the risk of endotracheal intubation following established status epilepticus. Neurology. 2021;96:e2372–86.
- Baumann SM, Semmlack S, Hunziker S, Kaplan PW, De Marchis GM, Rüegg S, et al. Prediction of postictal delirium following status epilepticus in the ICU: first insights of an observational cohort study. Crit Care Med. 2021;49:e1241–51.
- Zeidan S, Rohaut B, Outin H, Bolgert F, Houot M, Demoule A, et al. Not all patients with convulsive status epilepticus intubated in pre-hospital settings meet the criteria for refractory status epilepticus. Seizure. 2021;88:29–35.
- 9. Beuchat I, Rosenow F, Kellinghaus C, Trinka E, Unterberger I, Rüegg S, et al. Refractory status epilepticus: risk factors and analysis of intubation in the multicenter SENSE registry. Neurology. 2022;99:e1824–34.
- Alvarez V, Lee JW, Westover MB, Drislane FW, Novy J, Faouzi M, et al. Therapeutic coma for status epilepticus: differing practices in a prospective multicenter study. Neurology. 2016;87:1650–9.
- 11. Kellinghaus C, Rossetti AO, Trinka E, Lang N, May TW, Unterberger I, et al. Factors predicting cessation of status epilepticus in clinical practice: data from a prospective observational registry (SENSE). Ann Neurol. 2019;85:421–32.