Status Epilepticus

Section Editor: seat open
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Version 0.1 · Last reviewed 2026-07-19

Disclaimer: This protocol is an educational reference intended to support — not replace — institutional policy, pharmacy and therapeutics review, and individual clinical judgment. Verify current dosing, contraindications, and local formulary/practice constraints before adopting into an EMR or using in patient care.

Overview

Status epilepticus (SE) is a neurological emergency with mortality rising sharply as it becomes refractory (RSE) or super-refractory (SRSE). Time to treatment drives outcome, so this protocol is organized as a time-anchored escalation ladder. A key mechanistic point that explains why the ladder works this way: ongoing seizure activity causes GABA-A receptors to internalize (reducing benzodiazepine efficacy over time) while NMDA receptors are upregulated — which is why ketamine, an NMDA antagonist, has become an increasingly used option once GABAergic agents (benzodiazepines, then propofol/midazolam infusions) stop working.

Table 1. Definitions

TERM	DEFINITION
Status epilepticus (SE)	Continuous or intermittent seizures > 5 minutes without return to baseline
Refractory SE (RSE)	Persists despite adequate benzodiazepine + one appropriate ASM
Super-refractory SE (SRSE)	Persists or recurs despite ≥ 24 hours of anesthetic (continuous infusion) treatment
NORSE	New-onset refractory SE in a previously healthy person without an obvious acute cause
FIRES	NORSE subtype preceded by a febrile illness 1–14 days before onset

Steps

01 Recognize and Time-Stamp Onset

- Document time zero — every subsequent step is time-anchored to it.
- Protect the airway, position the patient, check fingerstick glucose and vitals immediately.
- Convulsive SE is a clinical diagnosis; nonconvulsive SE requires EEG (Step 4) — don't wait for EEG to start convulsive-SE treatment.

02 First-Line — Benzodiazepine (Give Promptly, Don't Underdose)

- IV lorazepam, IV/IM/buccal midazolam, or IV/rectal diazepam — choice depends on access; the priority is giving an adequate dose fast, not which specific agent.

03 Second-Line — Non-Sedating ASM (~10–30 min if seizures persist)

- (Fos)phenytoin, levetiracetam, or valproate — trial evidence suggests roughly comparable efficacy between these options.
- Lacosamide and brivaracetam are increasingly used alternatives.

04 Diagnose Nonconvulsive SE with EEG When Uncertain

- If convulsions stop but the patient doesn't return to baseline, or there's diagnostic uncertainty, obtain EEG.
- In the ICU, more than 90% of seizures/SE are nonconvulsive — only detectable with EEG. Conversely, most abnormal movements in ICU patients are **not** seizures — video-EEG prevents both under- and over-treatment.

05 Refractory SE — Continuous Infusion Anesthetic

- SE persisting despite benzodiazepine + one non-sedating ASM = RSE.
- Intubate, start a continuous infusion anesthetic drug (CIAD) — midazolam or propofol are the most commonly used first-line agents — and start continuous EEG (Step 8).
- If intubating, see Step 10 on induction agent choice.

06 Super-Refractory SE — Escalate

- SE persisting or recurring despite ≥ 24 hours of anesthetic infusion = SRSE.
- Options: additional non-sedating ASM trials, **ketamine** (Step 7), or barbiturates (pentobarbital/thiopental) — evidence comparing these head-to-head remains limited; choice is individualized.

07 Consider Ketamine Specifically

- Rationale: as GABA-A receptors internalize with prolonged SE, efficacy of GABAergic agents (benzodiazepines, midazolam, propofol) declines, while NMDA receptors are upregulated — ketamine works by a complementary, non-GABAergic mechanism.
- Reported dosing in case series: bolus averaging ~0.9–2 mg/kg, infusion starting around 10 mcg/kg/min and titrated (case series report ranges up to 20–30 mcg/kg/min, or reported in some series as ~1–2 mg/kg/h); confirm against current formulary guidance before building into an order set.
- Associated with hemodynamic stability (stable MAP, reduced vasopressor requirement) compared with GABAergic infusions — a practical advantage in hemodynamically fragile patients.
- Can be used **without intubation** in selected patients without respiratory compromise, particularly focal seizures — a meaningful option to avoid or delay intubation when appropriate, though most published experience remains as an adjunct in ventilated patients.

08 Continuous EEG (cEEG) Throughout RSE/SRSE Management

- Strongly recommended for any patient receiving anesthetics for SE.
- Recording up to 48 hours may be needed to detect 95% of seizures/SE in ICU patients — a single short EEG is not sufficient to rule out ongoing nonconvulsive seizures.

09 Identify and Treat the Underlying Etiology in Parallel

- Common causes: cerebrovascular disease (acute or chronic), brain tumor, trauma, toxic-metabolic disturbance, anoxic-ischemic encephalopathy, infection.
- If no clear cause in a previously healthy patient, consider a NORSE/FIRES workup (autoimmune and infectious encephalitis evaluation).
- Keep psychogenic non-epileptic events on the differential, especially for prolonged convulsions with forced eye closure and no desaturation or lactate rise — up to 10% of patients with prolonged convulsions in trial populations had psychogenic events, and over-treating them causes iatrogenic harm.

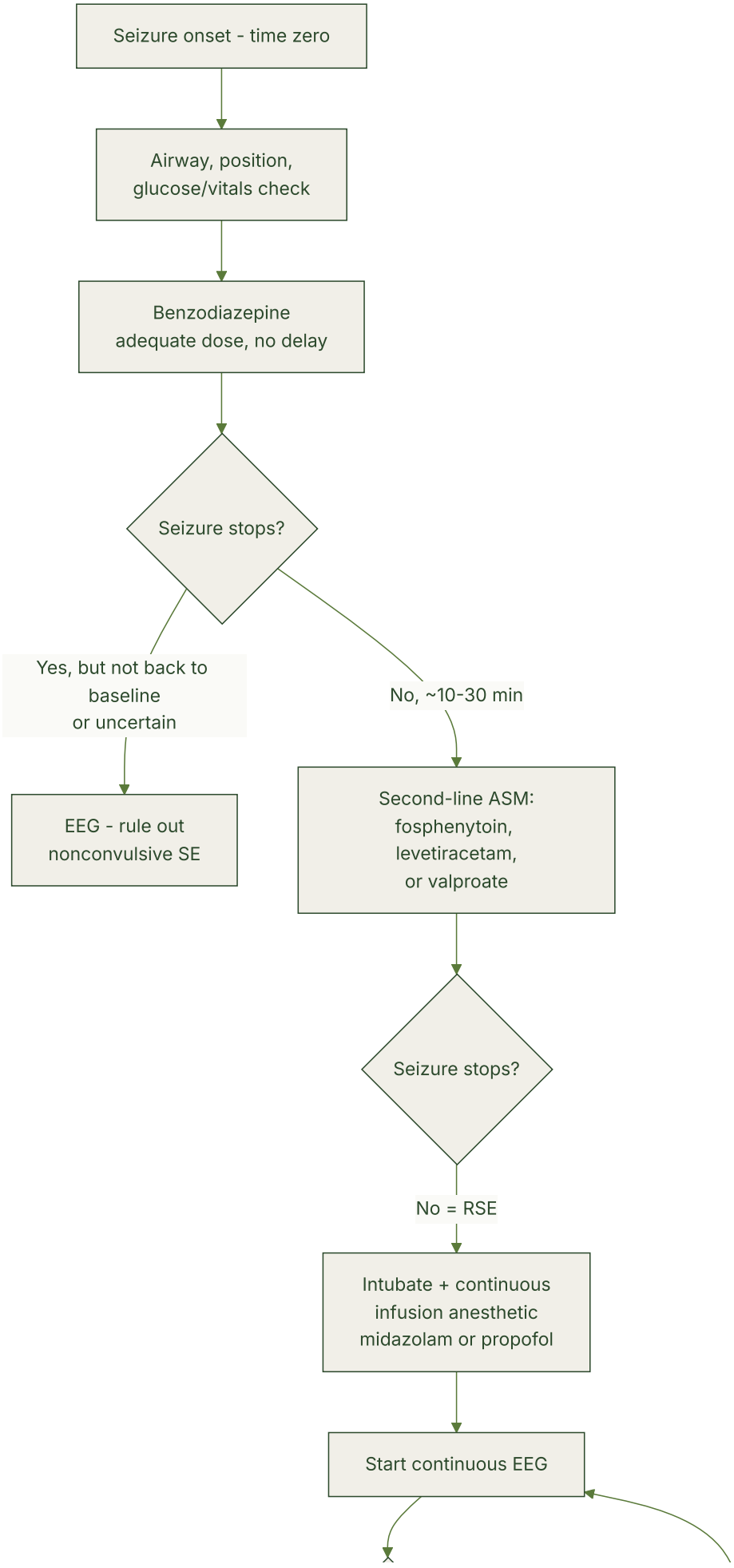
10 If Intubating, Choose the Induction Agent Carefully

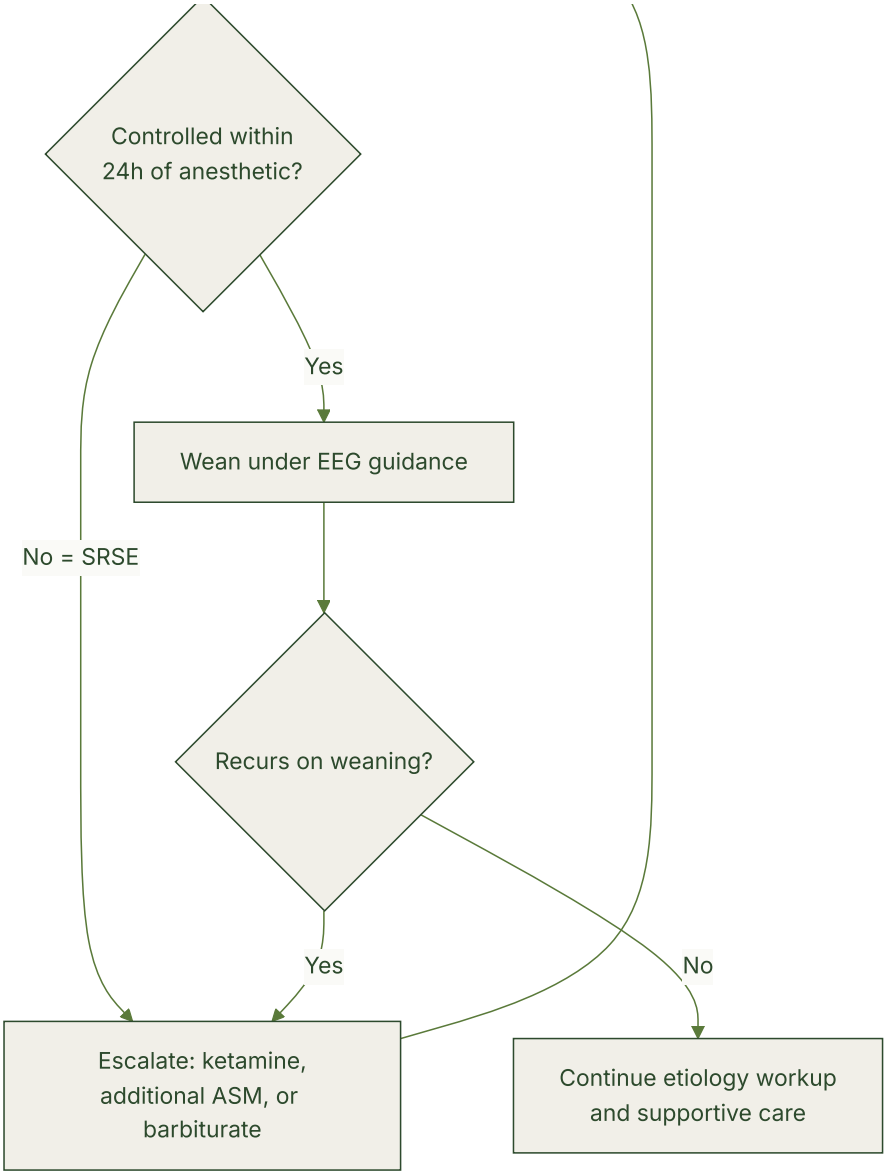
- A large propensity-matched study found etomidate associated with increased mortality compared with ketamine for induction in critically ill patients.
- Ketamine offers a dual benefit here — hemodynamically favorable induction plus a complementary antiseizure mechanism — and is a reasonable preferred induction agent in this population absent a specific contraindication.

11 Wean Anesthetic Infusions Under EEG Guidance

- Taper cautiously with continuous EEG running — recurrence during or after weaning is what defines SRSE and should prompt re-escalation rather than a repeat full taper attempt without a plan change.

Algorithm


Seizure onset - time zero
Airway, position, glucose/vitals check
Benzodiazepine adequate dose, no delay
Seizure stops?
Yes, but not back to baseline or uncertain
No, ~10-30 min
EEG - rule out nonconvulsive SE
Second-line ASM: fosphenytoin, levetiracetam, or valproate
Seizure stops?
No = RSE
Intubate + continuous infusion anesthetic midazolam or propofol
Start continuous EEG



EMR Order Set

PHYSICIAN ORDERS

- SE order set trigger, capturing time-zero.
- Benzodiazepine order (weight-based, agent per access route available).
- Second-line ASM order (fosphenytoin/levetiracetam/valproate selection).
- RSE escalation order bundle: intubation, continuous infusion anesthetic, neurology/neurocritical care consult, continuous EEG order.

- SRSE escalation order (ketamine or barbiturate infusion), with intubation induction-agent preference (ketamine over etomidate) noted.

NURSING ORDERS

- Time-zero and seizure-activity documentation (structured field).
- Vitals/glucose check at recognition.
- Coordinate EEG tech for continuous EEG setup and document start/interruption times.

PHARMACY ORDERS

- Weight-based dosing verification for benzodiazepine, ASM, and anesthetic/ketamine infusions.
- Renal/hepatic dose adjustment check for ASM selection.

Build notes — time-zero, each escalation tier's start time, and cEEG start time should be structured/timestamped fields so time-to-benzodiazepine, time-to-second-line-ASM, and time-to-cEEG can be pulled as metrics automatically.

Adoption Notes

- **Continuous EEG capability is a prerequisite**, not an optional add-on — confirm tech coverage and remote-read availability before building the RSE/SRSE escalation tiers into the order set.
- Build a neurology/neurocritical care consult trigger directly into the RSE escalation bundle (Step 5) rather than relying on a separate manual consult request.
- Ketamine for SE is less familiar to some ICU nursing/pharmacy staff than propofol/midazolam — include specific titration education before go-live, and confirm formulary stock.

Success Metrics & Monitoring

Time to first benzodiazepine, time to second-line ASM, time to continuous EEG initiation, seizure cessation rate within 24 hours of anesthetic/ketamine initiation, ICU length of stay, and mortality. Track via the critical care database and EEG lab records; review monthly during rollout.

Suggested Reading

1 Rossetti AO, Claassen J, Gaspard N. Status epilepticus in the ICU. *Intensive Care Med*. 2024;50(1):1–16. doi:10.1007/s00134-023-07263-w. Primary current review this protocol's escalation ladder is built from, including the RSE/SRSE definitions and cEEG recommendations.

2 Au YK, Kananeh MF, Rahangdale R, et al. Treatment of Refractory Status Epilepticus With Continuous Intravenous Anesthetic Drugs: A Systematic Review. *JAMA Neurol*. 2024;81(5):534–548. doi:10.1001/jamaneurol.2024.0108. Largest systematic comparison of CIAD choice (midazolam, propofol, pentobarbital, thiopental, ketamine) for RSE to date — evidence remains limited on optimal choice.

3 Alkhachroum A, Der-Nigoghossian CA, Mathews E, et al. Ketamine to treat super-refractory status epilepticus. *Neurology*. 2020;95(17):e2286–e2294. doi:10.1212/WNL.0000000000010611. Source for the hemodynamic-stability rationale (stable MAP, reduced vasopressor need) behind Step 7.

4 Kimmons LA, Alzayadneh M, Metter EJ, Alsherbini K. Safety and Efficacy of Ketamine Without Intubation in the Management of Refractory Seizures: A Case Series. *Neurocrit Care*. 2024;40(2):689–697. doi:10.1007/s12028-023-01811-4. Supports the non-intubated ketamine option in Step 7 for selected patients.

5 Caranzano L, Novy J, Rossetti AO. Ketamine in adult super-refractory status epilepticus: Efficacy analysis on a prospective registry. *Acta Neurol Scand*. 2022;145(6):737–742. doi:10.1111/ane.13610. Prospective (not just retrospective/case-series) ketamine efficacy data.

6 Wunsch H, Bosch NA, Law AC, et al. Evaluation of Etomidate Use and Association with Mortality Compared with Ketamine among Critically Ill Patients. *Am J Respir Crit Care Med*. 2024;210(10):1243–1251. doi:10.1164/rccm.202404-0813OC. Source for the induction-agent caution in Step 10.

Revision History

VERSION	DATE	EDITOR	SUMMARY
0.1	2026-07-19	FunctionalHealth editorial team	Initial version grounded in the six papers in the local Seizure source folder