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SEPSIS-ASSOCIATED ENCEPHALOPATHY AND DELIRIUM IN ADULT CRITICAL CARE: A MULTI DISCIPLINARY OF MEDICAL AND PARAMEDIC PERSPECTIVE FROM PREHOSPITAL RECOGNITION TO LONG-TERM OUTCOMES

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Abstract
Sepsis-associated encephalopathy (SAE) and sepsis-associated delirium (SAD) represent common forms of acute brain dysfunction in patients with sepsis and are strongly associated with short- and long-term morbidity and mortality . These syndromes arise from a complex interplay of systemic inflammation, microcirculatory failure, blood–brain barrier disruption, and dysregulated neurotransmission rather than direct central nervous system infection . Clinically, SAE spans a spectrum from subtle inattention and sleep–wake cycle disturbance to profound coma, while delirium is the dominant bedside manifestation in many patients . Accumulating evidence demonstrates that the duration and severity of delirium are independently associated with long-term cognitive impairment, functional disability, and the development of post-intensive care syndrome (PICS) . Because care of these patients is distributed across the prehospital, emergency, intensive care, psychiatric, laboratory, and nursing domains, an integrated multidisciplinary approach is required to optimize outcomes. This narrative review synthesizes current knowledge on mechanisms, diagnosis, and management of SAE and SAD from the perspectives of psychiatrist consultants, paramedics, adult critical care nurses, medical laboratory specialists, and nursing technicians. We summarize key epidemiologic data; outline contemporary concepts of pathophysiology with an emphasis on neuroinflammation and biomarkers; discuss prehospital recognition of sepsis and altered mental status; review guideline-based intensive care unit (ICU) strategies for pain, agitation, sedation, delirium, immobility, and sleep (PADIS); and highlight the roles of consultation–liaison psychiatry and the clinical laboratory in assessment and follow-up . Finally, we describe the long-term consequences of SAE within the broader construct of PICS and propose practical multidisciplinary pathways to improve prevention, early detection, and rehabilitation. Understanding SAE and SAD as shared responsibilities across disciplines is essential to reduce the substantial neurologic and psychological burden borne by survivors of sepsis and their families.
Keywords: Sepsis-associated encephalopathy, delirium, intensive care, paramedic, psychiatry, biomarkers, post-intensive care syndrome.

BACKGROUND

Sepsis is defined by the Third International Consensus (Sepsis-3) as life-threatening organ dysfunction caused by a dysregulated host response to infection [1]. This definition operationalizes organ dysfunction as an acute increase of at least 2 points in the Sequential Organ Failure Assessment (SOFA) score and underscores that sepsis is a syndrome of host–pathogen interaction rather than infection alone. Globally, recent estimates suggest tens of millions of sepsis cases and substantial in-hospital mortality each year, with survivors frequently experiencing

long-term physical, cognitive, and psychological sequelae. The central and peripheral nervous systems are particularly vulnerable in sepsis. Neurologic complications range from SAE and delirium to seizures, critical illness polyneuromyopathy, and long-lasting cognitive deficits. SAE is traditionally defined as a diffuse brain dysfunction occurring in the context of sepsis in the absence of direct central nervous system infection or other primary structural brain disease. Clinically, SAE is highly heterogeneous: patients may present with fluctuating inattention, disorganized thinking, psychomotor agitation or retardation, or unresponsiveness, and focal deficits should prompt investigation for alternative diagnoses such as stroke or encephalitis.[2]

Delirium is a form of acute brain dysfunction characterized by a disturbance in attention and awareness, developing over a short period and tending to fluctuate, often accompanied by additional cognitive disturbance [3]. In ICUs, delirium affects up to half of critically ill adults and is independently associated with increased mortality, longer mechanical ventilation, prolonged length of stay, greater healthcare costs, and subsequent cognitive impairment. Sepsis is one of the strongest precipitants of delirium, and delirium related to sepsis is often categorized as SAD or as part of the broader construct of SAE. Importantly for practice, delirium and coma are not benign, self-limited epiphenomena but powerful prognostic markers and potential therapeutic targets across the continuum of sepsis care.

Historically, SAE was under-recognized, in part because bedside neurologic assessment is challenging in mechanically ventilated, sedated patients and because no single biomarker or imaging feature is diagnostic [5]. Over the past two decades, however, advances in delirium screening tools, brain imaging, neurophysiology, and biomarkers, coupled with large cohort studies, have transformed understanding of epidemiology, mechanisms, and consequences of sepsis-related brain dysfunction. At the same time, critical care practice has shifted from deep, benzodiazepine-based sedation toward lighter, analgesia-first sedation strategies and structured bundles such as the ABCDEF approach, which emphasize routine delirium monitoring, early mobilization, and family engagement. These developments create a strong rationale for a multidisciplinary synthesis targeted at clinicians working in psychiatry, prehospital care, critical care nursing, laboratory medicine, and general nursing practice [10].

LITERATURE REVIEW

We conducted a targeted narrative review to inform this article, focusing on human and translational studies relevant to SAE, SAD, ICU delirium, prehospital sepsis recognition, biomarkers of sepsis-related brain injury, and post-intensive care outcomes. Key primary and secondary sources were identified through searches of PubMed and PubMed Central using combinations of terms including ‘sepsis-associated encephalopathy, sepsis-associated delirium’, neurologic complications of sepsis’, ICU delirium’, post-intensive care syndrome’, paramedic sepsis recognition’, and ‘neurofilament’ or ‘S100B’ and ‘sepsis’. Seminal guideline documents and high-impact reviews, such as Sepsis-3, the 2018 Society of Critical Care Medicine PADIS guideline, and the 2021 Surviving Sepsis Campaign recommendations, were also prioritized [4].

Recent comprehensive reviews of SAE and its spectrum provided core pathophysiologic and diagnostic frameworks, particularly the work by Chung and colleagues on the progression from delirium to dementia and by Zampieri and colleagues on the broader clinical spectrum of SAE [3]. The dedicated narrative review on SAD by Atterton and co-workers offered focused insight into sepsis-triggered delirium and its overlap with general ICU delirium literature. Reviews of neurologic complications of sepsis and of delirium management in critical illness were used to integrate evidence on peripheral neuromuscular involvement and general delirium strategies into the sepsis context.

For long-term outcomes, we drew on observational cohort studies and narrative reviews of PICS, which describe the high prevalence of persistent physical, cognitive, and psychological impairments among ICU survivors, including those with sepsis [10]. Prehospital and emergency perspectives were informed by systematic reviews and primary studies addressing paramedic recognition of sepsis, early warning scores, and delirium identification barriers in EMS and emergency departments. Biomarker sections were guided by systematic reviews and meta-analyses of S100B, endothelial glycocalyx-derived molecules, and neurofilament light chain in SAE, as well as broader sepsis biomarker editorials. Where high-quality randomized trials were lacking, we relied on carefully conducted observational studies, mechanistic animal work, and expert consensus, explicitly noting areas of uncertainty.

Definitions and diagnostic concepts

The Sepsis-3 task force redefined sepsis as life-threatening organ dysfunction caused by a dysregulated host response to infection and septic shock as a subset characterized by vasopressor-dependent hypotension and elevated lactate despite adequate fluid resuscitation. Neurologic dysfunction in this framework is one component of organ failure and may manifest as delirium, coma, seizures, or more subtle cognitive and affective changes.

SAE refers specifically to diffuse cerebral dysfunction temporally associated with sepsis, in the absence of direct CNS infection, structural brain lesions, or alternative metabolic or toxic encephalopathies. Because sepsis frequently coexists with hypoxia, renal and hepatic failure, and exposure to psychoactive medications, SAE is fundamentally a diagnosis of exclusion that requires systematic evaluation for primary neurologic diseases such as stroke, meningitis, encephalitis, status epilepticus, and posterior reversible encephalopathy syndrome [5].

Delirium is defined in psychiatric nosology as an acute, fluctuating disturbance in attention and awareness with additional cognitive disturbance; motor subtypes include hyperactive, hypoactive, and mixed forms. In the ICU,

validated tools such as the Confusion Assessment Method for the ICU (CAM-ICU) and the Intensive Care Delirium Screening Checklist (ICDSC) are recommended by PADIS and subsequent guidelines for routine delirium screening, with pooled sensitivities around 80% and specificities exceeding 90% in meta-analyses [13]. SAD describes delirium occurring in the context of sepsis; it is conceptually nested within SAE but emphasizes bedside delirium phenomenology.

From a practical standpoint, clinicians should conceptualize SAE as a spectrum that includes early subtle inattention and sleep–wake inversion, overt delirium, and, at the extreme, coma and seizures. Importantly, delirium and coma are not mutually exclusive phenomena but overlapping manifestations of acute brain dysfunction; many cohort studies now analyze 'delirium- and coma-free days' as a composite outcome [8]. Recognition that even mild decreases in Glasgow Coma Scale scores in septic patients predict worse outcomes underscores the need for high vigilance among paramedics, ward nurses, intensivists, and psychiatrists alike.

Epidemiology and burden

SAE is considered the most common form of encephalopathy in the ICU, affecting up to half of patients with sepsis, with even higher rates reported in those with bacteremia or multi-organ failure. Large registry and cohort analyses demonstrate that encephalopathy in sepsis develops early, often before full diagnostic criteria for sepsis are met, and its presence is associated with increased ICU and hospital mortality. Mortality rates approaching 50–60% have been described in septic patients with severe neurologic dysfunction compared with substantially lower rates in those without encephalopathy.

Delirium is common across etiologies of critical illness, but sepsis appears to be a particularly potent risk factor. In mixed ICU populations, delirium prevalence ranges from 20% to more than 50%, and delirium incidence is closely tied to illness severity, exposure to benzodiazepines, depth of sedation, and the presence of sepsis or shock. Duration of delirium is independently associated with worse global cognition at 3 and 12 months, greater functional dependence, and reduced return to work in survivors. Importantly, hypoactive delirium, which may be misinterpreted as depression or fatigue, is at least as common as hyperactive forms and carries similar or worse prognostic implications [7].

Beyond the hospital stay, sepsis survivors with SAE or prolonged delirium are at high risk of developing PICS, characterized by new or worsening physical, cognitive, and mental health problems persisting beyond acute care. Narrative reviews and cohort studies of ICU survivors report that more than half of patients experience at least one PICS domain—commonly ICU-acquired weakness, cognitive slowing, memory impairment, anxiety, depression, or post-traumatic stress symptoms—months to years after discharge. These deficits substantially impair health-related quality of life, increase caregiver burden, and generate substantial healthcare utilization and socioeconomic costs.

Pathophysiology of sepsis-associated brain dysfunction

The pathophysiology of SAE and SAD is multifactorial and incompletely elucidated. Current models emphasize synergistic contributions from cerebral hypoperfusion and microcirculatory failure, blood–brain barrier disruption, neuroinflammation with microglial and astrocytic activation, mitochondrial dysfunction, oxidative stress, and dysregulated neurotransmission [8].

Sepsis impairs both macro- and microcirculatory blood flow to the brain. Transcranial Doppler and perfusion studies demonstrate impaired cerebral autoregulation and reduced capillary density in SAE, rendering the brain vulnerable to fluctuations in blood pressure and systemic hypoxia. Autopsy and MRI series reveal patchy ischemic and hemorrhagic lesions, particularly in watershed regions and white matter, alongside microglial activation in grey and white matter [9].

Systemic inflammation activates cerebral endothelial cells, increasing expression of adhesion molecules such as intercellular adhesion molecule-1 and promoting leukocyte trafficking into perivascular spaces. This process, together with oxidative stress and matrix metalloproteinase activation, disrupts tight junctions and compromises the blood–brain barrier, permitting cytokines and circulating toxins to access the parenchyma. Microglia and astrocytes respond with a pro-inflammatory phenotype, releasing additional cytokines and reactive oxygen species that further perturb synaptic function and neuronal survival [15].

At the cellular level, mitochondrial dysfunction appears central. Experimental sepsis models demonstrate reduced efficiency of oxidative phosphorylation, decreased activity of respiratory chain enzymes, and increased susceptibility to apoptosis in hippocampal and cortical neurons. These changes contribute to an 'energy crisis' that may underlie cognitive slowing and vulnerability to secondary insults.

Neurotransmitter systems are also disrupted. Clinical and experimental studies implicate alterations in cholinergic, gamma-aminobutyric acid, dopaminergic, noradrenergic, and serotonergic signaling in the genesis of delirium, although attempts to modulate these pathways pharmacologically (for example, with cholinesterase inhibitors) have not improved outcomes and in some cases worsened mortality. Disturbances in tryptophan and tyrosine availability, which serve as precursors for serotonin and catecholamines, have been associated with delirium risk in ICU cohorts [31].

Biomarker studies add further support to neuronal and endothelial injury in SAE. Serum S100B, a glial protein, is modestly elevated in many SAE patients and has been associated with encephalopathy and worse outcomes in meta-analysis, although its specificity is limited [38]. Endothelial glycocalyx components such as soluble vascular and intercellular adhesion molecules are higher in septic patients with encephalopathy than in those without, supporting a role for endothelial injury. More recently, neurofilament light chain, a cytoskeletal protein released with axonal damage, has emerged as a promising biomarker: elevated serum neurofilament levels have been

described in sepsis and correlate with neurologic injury in broader critical care populations. However, none of these biomarkers alone is sufficient for diagnosis in clinical practice, and further validation in well-characterized SAE cohorts is required.

Prehospital and emergency perspectives

Paramedics and other prehospital providers are often the first clinicians to encounter patients with evolving sepsis and acute changes in mental status. Early recognition of sepsis in the field can shorten time to antibiotics and hemodynamic resuscitation in the emergency department, which is associated with improved outcomes [33]. Prospective observational work suggests that, when equipped with structured sepsis screening tools, paramedics can identify sepsis with sensitivities in the range of 70–80% and specificities around 75–80% compared with emergency physician diagnoses.

Several prehospital studies have examined early warning scores and paramedic impressions as predictors of sepsis and adverse outcomes. National Early Warning Score–based approaches and tailored sepsis screening tools improve detection compared with clinical gestalt alone, although positive predictive values remain modest because many acutely unwell patients do not ultimately meet sepsis criteria. Nevertheless, EMS-initiated sepsis alerts to receiving hospitals are associated with shorter times to implementation of resuscitation bundles, including antibiotics, fluids, and intensive monitoring.

From a neurologic standpoint, altered mental status in the prehospital environment should prompt a structured assessment of airway, breathing, circulation, glucose, and temperature, alongside focused history from family or caregivers to establish baseline cognition [35]. Qualitative work with EMS, nursing, and physician providers highlights that lack of knowledge of a patient's premorbid cognitive status is a major barrier to delirium recognition; conversely, collateral information from family or care-home staff is often decisive in identifying acute cognitive change. Educational initiatives for paramedics increasingly emphasize that delirium is a medical emergency and that its hyperactive and hypoactive forms warrant urgent evaluation for underlying infection, hypoxia, metabolic derangement, or drug toxicity [17].

For psychiatrist consultants and critical care teams, appreciation of prehospital events is vital. Documentation of prehospital vital signs, mental status, and timing of symptom onset can help differentiate chronic neurocognitive disorders from acute SAE, inform risk stratification, and guide early goals-of-care discussions. In practice, simple steps such as standardized handover templates that include baseline cognition, recent functional decline, and use of psychoactive medications can materially improve delirium recognition and management throughout the admission [20].

Adult critical care nursing perspective

Adult critical care nurses play a central role in the prevention, detection, and management of SAE and SAD. PADIS and subsequent national guidelines recommend that all ICU patients be routinely assessed for pain, agitation, level of consciousness, and delirium using validated tools, and that sedation strategies prioritize analgesia-first, light sedation, and early mobilization. Implementation studies demonstrate that higher compliance with the ABCDEF bundle—Assess pain; Both spontaneous awakening and breathing trials; Choice of analgesia and sedation; Delirium assessment, prevention, and management; Early mobility and exercise; Family engagement—is associated with lower mortality, shorter mechanical ventilation, and fewer delirium and coma days [21].

In delirium prevention and management, non-pharmacologic measures are foundational. These include repeated reorientation, optimization of sleep–wake cycles, avoidance of sensory deprivation through provision of glasses and hearing aids, minimizing unnecessary noise and nocturnal interventions, promoting early mobilization, and removing or avoiding physical restraints and invasive devices where possible. Randomized trials and quality improvement projects have shown that simple interventions such as earplugs, eye masks, and sleep protocols can reduce the incidence or severity of delirium in some ICU populations [14].

Sedation practices have profound implications for SAE and SAD. Benzodiazepines are consistently identified as modifiable risk factors for ICU delirium and should generally be avoided as first-line sedatives in favor of propofol or dexmedetomidine, aiming for light rather than deep sedation whenever clinically feasible. In a pivotal randomized trial in septic patients, dexmedetomidine-based sedation was associated with more delirium- and coma-free days and lower 28-day mortality compared with lorazepam, although subsequent larger trials have yielded more nuanced results. Nurses operationalize these strategies through protocolized sedation targeting, daily sedation interruptions or nurse-driven titration to a Richmond Agitation-Sedation Scale of around 0 to −2, and close monitoring for oversedation and withdrawal.

Critical care nurses are also key in implementing structured delirium screening using tools such as CAM-ICU and ICDSC. Despite strong evidence and guidelines, surveys suggest that delirium is still under-monitored in many ICUs, and even when monitored, documentation may not trigger systematic evaluation or intervention. Embedding delirium assessments into nursing observation charts and electronic health records, coupled with education and feedback, can improve reliability and foster a culture in which 'thinking delirium' is part of routine care [24].

Psychiatric perspective

Consultation–liaison psychiatrists frequently become involved when delirium manifests with severe agitation, hallucinations, or behavioral disturbance, or when hypoactive states raise concern for depression or catatonia. In the context of sepsis, psychiatric input is most effective when integrated early and collaboratively rather than reserved solely for pharmacologic rescue [26].

From a diagnostic standpoint, psychiatrists can assist in differentiating delirium from primary psychotic or mood disorders, substance withdrawal, neurocognitive disorders, and functional neurological presentations. They can help interpret collateral history, cognitive testing, and delirium scales, and advise on the relevance of premorbid psychiatric illness or psychotropic medications to the current presentation. Close attention to motoric subtype is important: hypoactive delirium may be mislabelled as depression, leading to potentially harmful introduction of sedating antidepressants or antipsychotics instead of focusing on underlying medical precipitants.

Pharmacologic management of agitation in SAD remains controversial. Randomized trials have failed to show that haloperidol or atypical antipsychotics shorten delirium duration, reduce ICU length of stay, or improve survival, although they may remain useful for short-term control of dangerous agitation or psychosis. PADIS therefore advises against routine use of antipsychotics for delirium treatment and emphasizes non-pharmacologic strategies and optimization of analgesia, sedation, and sleep. When medications are used, psychiatrists can help select agents with favorable cardiometabolic and extrapyramidal risk profiles, use the lowest effective doses, and ensure timely de-escalation to avoid prolonged exposure after ICU discharge [30].

Psychiatrists also have a role in the longitudinal care of sepsis survivors. PICS encompasses depression, anxiety, post-traumatic stress symptoms, and cognitive impairment that often overlap and may require structured assessment and treatment in post-ICU clinics or community mental health settings. Cognitive–behavioral therapy, trauma-focused interventions, judicious use of antidepressants and anxiolytics, and coordination with rehabilitation teams can mitigate some of the long-term psychological burden experienced by patients and families [12].

Medical laboratory perspective

Medical laboratory specialists underpin nearly every aspect of sepsis care, from confirming infection and guiding antimicrobial therapy to quantifying organ dysfunction and exploring candidate neurologic biomarkers. Standard sepsis panels include blood cultures, complete blood count, inflammatory markers, renal and hepatic function, coagulation studies, and serum lactate, all of which inform sepsis diagnosis and severity assessment and may influence cerebral perfusion and risk of SAE.

Beyond routine tests, several laboratory markers have specific relevance to sepsis-related brain dysfunction. Serum S100B and neuron-specific enolase are elevated in many patients with SAE and have been associated with encephalopathy and worse neurologic outcomes, although their specificity is limited because extracerebral sources and generalized critical illness can also raise levels. Endothelial glycocalyx-associated molecules such as soluble intercellular and vascular adhesion molecules are higher in septic patients with encephalopathy than in those without, reflecting endothelial injury and blood–brain barrier disruption [39].

Neurofilament light chain has recently emerged as a particularly promising biomarker. As a structural component of myelinated axons, neurofilament light enters cerebrospinal fluid and blood following axonal damage; highly sensitive single-molecule array assays now allow its quantification in serum [40]. Early studies in sepsis and mixed critical illness populations suggest that elevated serum neurofilament concentrations correlate with the presence and severity of encephalopathy and may predict long-term cognitive impairment. Laboratory specialists can help standardize sampling protocols, interpret neurofilament values in the context of age and comorbid neurodegenerative disease, and advise clinicians on the current limitations of these tests.

From an operational perspective, laboratory professionals also contribute to antimicrobial stewardship by providing rapid organism identification and susceptibility data, supporting Surviving Sepsis Campaign recommendations for timely, targeted therapy [2]. Reducing unnecessary broad-spectrum antibiotic exposure may indirectly benefit brain function by lowering risks of nephrotoxicity, hepatotoxicity, Clostridioides difficile infection, and drug interactions that complicate delirium management.

Nursing technician and paramedics staff perspective

Nursing technicians and other bedside paramedics staff are essential yet sometimes under-recognized members of the team caring for patients with SAE and SAD. Their continuous presence at the bedside positions them to detect early changes in mental status, behavior, sleep patterns, and functional ability that may herald evolving encephalopathy or delirium.

Practical contributions include accurate measurement and documentation of vital signs, urine output, and fluid balance; timely reporting of new confusion, agitation, or unresponsiveness; assistance with mobilization and repositioning; and support of basic communication and orientation [15]. Protocols that empower nursing technicians to escalate concerns about acute cognitive changes for example, delirium triggers that prompt nurse or physician review can shorten recognition delays and initiate earlier investigation for sepsis progression, metabolic disturbances, or medication toxicity.

Paramedics staff also play a crucial role in implementing non-pharmacologic delirium-prevention bundles. Helping patients use glasses and hearing aids, facilitating daytime exposure to natural light, minimizing unnecessary overnight noise and handling, and engaging families in reorientation are low-technology interventions that require coordination across the care team. Targeted training that explains why delirium matters linking bedside observations to long-term cognitive and functional outcomes can enhance motivation and adherence to these practices [18].

Multidisciplinary care pathways and long-term outcomes

Given the complex, multisystem nature of SAE, coordinated multidisciplinary pathways are essential. During the

acute phase of sepsis, integration of Surviving Sepsis Campaign resuscitation bundles with PADIS-aligned ICU practices and systematic delirium screening offers the best current framework for reducing the incidence and duration of SAE and improving survival [14].

Key components of such pathways include early identification of sepsis in the prehospital and emergency settings; prompt antibiotics and source control; hemodynamic optimization; judicious use of vasopressors and ventilation strategies that avoid excessive sedation and hypoxia; routine use of pain, sedation, and delirium assessment tools; non-pharmacologic delirium-prevention bundles; and family engagement and communication about expected cognitive trajectories. Psychiatric, neuropsychological, and rehabilitation input should be sought early for patients with prolonged delirium, pre-existing cognitive impairment, or severe psychological distress.

Beyond ICU discharge, structured follow-up is increasingly recognized as vital. Post-ICU or post-sepsis clinics that bring together intensivists, internists, psychiatrists, psychologists, physiotherapists, and occupational therapists can systematically screen for PICS, educate patients and families, and coordinate rehabilitation plans. Narrative reviews and early cohort data suggest that such multidisciplinary models may improve functional outcomes and quality of life, although high-quality randomized evaluations remain limited. For many survivors, return to work, restoration of social roles, and support for family caregivers are as important as traditional biomedical endpoints.

CONCLUSION

SAE and SAD are highly prevalent, clinically important manifestations of sepsis that confer substantial short- and long-term risks for adult patients in critical care. They arise from a convergence of systemic inflammation, cerebral microcirculatory failure, blood–brain barrier disruption, and neurochemical dysregulation, and they cannot be fully understood or managed within any single professional silo. For psychiatrist consultants, paramedics, adult critical care nurses, medical laboratory specialists, and nursing technicians, recognizing SAE as a shared problem and aligning practice with guideline-supported, multidisciplinary pathways are key steps toward reducing its burden.

Evidence supports early prehospital and emergency recognition of sepsis and altered mental status; guideline-based hemodynamic and antimicrobial management; light, analgesia-focused sedation coupled with structured delirium monitoring; non-pharmacologic delirium-prevention bundles; cautious, sparing use of antipsychotics; and systematic post-ICU follow-up for PICS. Emerging biomarkers such as neurofilament light chain and advances in neuroimaging and electroencephalography may soon refine risk stratification and prognostication, but current practice can already be markedly improved through reliable implementation of existing tools and concepts.

Ultimately, improving outcomes for patients with SAE will depend on sustained collaboration across disciplines, continuous education of all bedside providers regarding delirium and PICS, and research that bridges mechanistic insights with pragmatic clinical interventions. By embedding neurologic and psychological outcomes into routine sepsis care, clinicians can move beyond survival alone toward preserving cognition, independence, and quality of life for survivors and their families.

Despite promising findings, most biomarkers lack sufficient specificity and are not yet recommended for routine clinical use.

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