Sedation, Delirium, and Cognitive Function After Critical Illness



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KEYWORDS

• Intensive care • Cognition • Delirium • Mechanical ventilation • Sedation

KEY POINTS

- Critically ill patients who are heavily sedated, especially with a benzodiazepine, are at high
 risk for delirium and other adverse outcomes.
- During critical illness, duration of delirium is an important, potentially modifiable predictor of long-term cognitive impairment.
- Clinicians should view delirium in a sedated ICU patient as a warning sign that patients may be experiencing brain injury, and they should reduce or eliminate sedation if possible.

INTRODUCTION

Cognition, defined broadly by the American Psychological Association¹ as "all forms of knowing and awareness, such as perceiving, conceiving, remembering, reasoning, judging, imagining, and problem solving," is frequently impaired during critical illness. A high percentage of critically ill patients are comatose or delirious when they are admitted to the ICU and those who are not are at high risk of developing these impairments in cognition during their ICU stay.

Among patients who survive their acute illness, coma and delirium typically resolve. For many years, clinicians mistakenly assumed that the oft-observed resolution of acute cognitive deficits meant that patients' cognition returned to baseline, but a growing body of literature has described an alarmingly high rate of cognitive impairment that persists for months to years for many survivors of critical illness. Patients and providers alike are now seeking to identify and target modifiable risk factors for this form of cognitive impairment, which this article refers to as "critical illness brain injury," with attempts to prevent and/or treat delirium being central in their efforts.

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Crit Care Clin 34 (2018) 585–598 https://doi.org/10.1016/j.ccc.2018.06.009 0749-0704/18/© 2018 Elsevier Inc. All rights reserved. Delirium has been consistently identified as a risk factor for critical illness brain injury,^{3,4} but ICU patients are exposed to a multitude of risk factors for delirium and it remains unclear which of these risk factors should be targeted to improve long-term cognitive outcomes. Because exposure to sedating medications—which are frequently used to treat unwanted yet common symptoms during critical illness⁵—is a risk factor for delirium that is directly controlled by clinicians, the relationship between sedation, delirium, and long-term cognition is of great interest to clinicians, researchers, and patients. This review describes the current body of evidence that informs our understanding of the relationships between sedation, delirium, and long-term cognition (Fig. 1).

SEDATION DURING CRITICAL ILLNESS

Critically ill patients are likely to experience anxiety and pain during their illness. ⁶ Clinicians, therefore, often treat ICU patients with sedatives and analgesics to alleviate anxiety, pain, and, in some cases, agitation. Although sedating medications provide an important benefit to many critically ill patients, it is well established that these drugs can also adversely impact outcomes in the ICU. Two decades ago, Kollef and colleagues ⁷ found that patients treated with continuous intravenous sedation experience delays in extubation and discharge from the ICU and hospital compared with those who received sedation via intermittent boluses.

Numerous studies in the past 20 years have confirmed these findings and demonstrated that heavy sedation not only is associated with prolonged ventilator and ICU stays but also with increased mortality. The sedation practice in intensive care evaluation (SPICE) investigations, for example, evaluated 703 mechanically ventilated ICU patients across 42 ICUs in Australia, New Zealand, Malaysia, and Singapore and found that, compared with light sedation, deeper sedation during the first 48 hours of an ICU admission was associated with delayed time to extubation and increased risk within 6 months of critical illness.⁸

Concerns over adverse effects of sedation prompted the study of a variety of approaches to safely deliver sedation to ICU patients. Strategies designed to promote light sedation have included sedation protocols that rely on sedation scales to guide

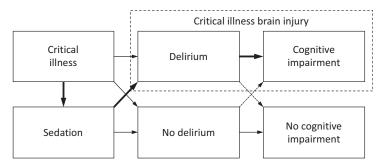


Fig. 1. Potential relationships between sedation, delirium, and cognitive impairment. Heavy arrows indicate associations identified in recent studies of general medical/surgical ICU patients—critical illness often results in exposure to sedating medications, many of which (especially when given in high doses) are associated with delirium, which in turn is associated with cognitive impairment that persists months to years after critical illness. Light and dashed arrows indicate the heterogeneity observed in studies of general medical/surgical ICU patients—not all critically patients who receive sedation develop delirium, and delirium is neither 100% sensitive nor 100% specific as a predictor of long-term cognitive impairment.

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