

Original Research Reports

Agitation, Delirium, and Cognitive Outcomes in Intracerebral Hemorrhage



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Background: Delirium predicts higher long-term cognitive morbidity. We previously identified a cohort of patients with spontaneous intracerebral hemorrhage and delirium and found worse outcomes in health-related quality of life (HRQoL) in the domain of cognitive function. **Objective:** We tested the hypothesis that agitation would have additional prognostic significance on later cognitive function HRQoL.

Methods: Prospective identification of 174 patients with acute intracerebral hemorrhage, measuring stroke severity, agitation, and delirium, with a standardized protocol and measures. HRQoL was assessed using the Neuro-QOL at 28 days, 3 months, and 1 year. Functional outcomes were measured with the modified Rankin Scale. **Results:** Among the 81 patients with

HRQoL follow-up data available, patients who had agitation and delirium had worse cognitive function HRQoL scores at 28 days (*T* scores for delirium with agitation 20.9 ± 7.3 , delirium without agitation 30.4 ± 16.5 , agitation without delirium 36.6 ± 17.5 , and neither agitated nor delirious 40.3 ± 15.9 ; $p = 0.03$) and at 1 year ($p = 0.006$). The effect persisted in mixed models after correction for severity of neurologic injury, age, and time of assessment ($p = 0.0006$) and was not associated with medication use, seizures, or infection. **Conclusions:** The presence of agitation with delirium in patients with intracerebral hemorrhage may predict higher risk of unfavorable cognitive outcomes up to 1 year later.

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Key words: cognition disorders, delirium, hyperkinesia, psychomotor agitation, quality of life, stroke.

INTRODUCTION

Hospitalized patients with delirium have high morbidity and mortality, and there has been increasing evidence of the particular impact on long-term cognitive function.^{1–3} Hyperactive, hypoactive, and mixed subtypes of delirium have been described both historically and in Diagnostic and Statistical Manual 5, but there are limited data describing the prognostic implications of motor subtypes on cognition.^{4–9} The etiology of delirium can be complex, and its varied

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Delirium and Cognitive Outcomes in ICH

pathophysiologic processes complicate study and can limit generalizability of outcomes.¹⁰ Although most reports describe delirium in patients with global conditions such as sepsis,¹¹ focal brain injuries such as neurological disorders are common, and delirium in this context is an interesting model because there is relatively limited systemic inflammation, infection, or confounding medication administration. Delirium has been demonstrated to be common in acute ischemic stroke, estimated at 11–50%, and presages poorer functional outcomes.^{12,13}

In the recent past, long-term stroke outcomes research was based largely on motor symptoms, but the National Institutes of Health (NIH) recently developed the Neuro-QOL and the Patient Reported Outcomes Measurement Information System to provide state-of-the-art outcomes that reflect the perspective of patients and caregivers,^{14,15} and these have been validated against the current standard for outcomes assessment. Using these validated measures on a cohort of patients with intracerebral hemorrhage (ICH, spontaneous bleeding into brain tissue), we previously reported that patients with delirium had poorer functional outcomes at 28 days, and worse cognitive function health-related quality of life (HRQoL) at 28 days, 3 months and 1 year than similar patients without delirium.¹⁶ We then hypothesized that motor agitation with delirium (hyperactive delirium) would have additional prognostic significance.

MATERIALS AND METHOD

We prospectively identified 174 patients with acute ICH admitted from December 2009 to October 2014. All patients were diagnosed with ICH by a board-certified neurologist using computed tomography. Patients were excluded if their ICH was attributable to trauma, hemorrhagic conversion of ischemic stroke, or structural lesions (aneurysm, tumor, arteriovenous malformation, or vessel dissection). Patients received nursing care with nonpharmacologic methods to prevent and address delirium, such as frequent reorientation and employing the participation of loved ones, as part of hospital protocol.

All patients with ICH were admitted to the Neuro/Spine ICU with a standardized order set. We prospectively recorded baseline demographic, past medical history, clinical data, and follow-up data.¹⁶

Electroencephalographic monitoring was routinely performed in unresponsive patients and interpreted by a board-certified epileptologist to evaluate for the presence of subclinical seizures. We assessed patients with the NIH Stroke Scale, a validated neurologic examination ranging from 0 (no deficit) to 42 (worst possible score), with a score of 8 or more indicating a moderately severe deficit.¹⁷ We also assessed the ICH Score, a validated severity of injury scale from 0 (least severe) to 6 (most severe).¹⁸

Delirium and Agitation Assessment

The Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) was used to assess delirium, which has been validated for use in patients with acute stroke and neurological injury, including ICH.^{19,12} As previously noted, a positive CAM-ICU indicated the presence of a change from the patient's new baseline mental status (established on admission after ICH symptom onset) plus inattention, and either an altered level of consciousness or disorganized thinking as previously described.

Level of arousal was assessed using the Richmond Agitation-Sedation Scale (RASS).²⁰ The RASS is scored from –5 (unresponsive) to +4 (combative, violent). For intubated patients, Neuro/Spine ICU protocol treatment goal was 0 (alert and calm) to –2 (briefly awakens with eye contact to voice). A RASS of 2 (frequent nonpurposeful movement or ventilator dys-synchrony) or greater was considered to indicate agitation.

The CAM-ICU and RASS were assessed twice per day by trained nursing staff during inpatient admission. CAM-ICU assessment and RASS assessment appear on the bedside ICU nurse's task list every shift and require a response. These methods have been previously described.¹⁶ We consider patients to have delirium with agitation if there was a positive CAM-ICU and RASS of 2 or more at any point during the hospital stay. Delirium without agitation indicates a positive CAM-ICU at any time with all RASS scores of less than 2 during the hospital stay. Agitation without delirium indicates a RASS of 2 or more, no positive CAM-ICU assessments, and at least 1 negative CAM-ICU assessment during the hospital stay, for example, the patient could be assessed with the CAM-ICU at least once. If the RASS remained less than 2 and all CAM-ICU assessments were negative

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