NEUROIMAGING IN DELIRIOUS INTENSIVE CARE UNIT PATIENTS:

A Preliminary Case Series Report

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ABSTRACT

Objective. There exists uncertainty regarding the role of magnetic resonance imaging in the evaluation of intensive care unit delirious patients. This case series describes preliminary magnetic resonance imaging findings obtained because of delirium, subsequent in-hospital clinical decisions, and post-discharge neurocognitive outcomes in intensive care unit survivors.

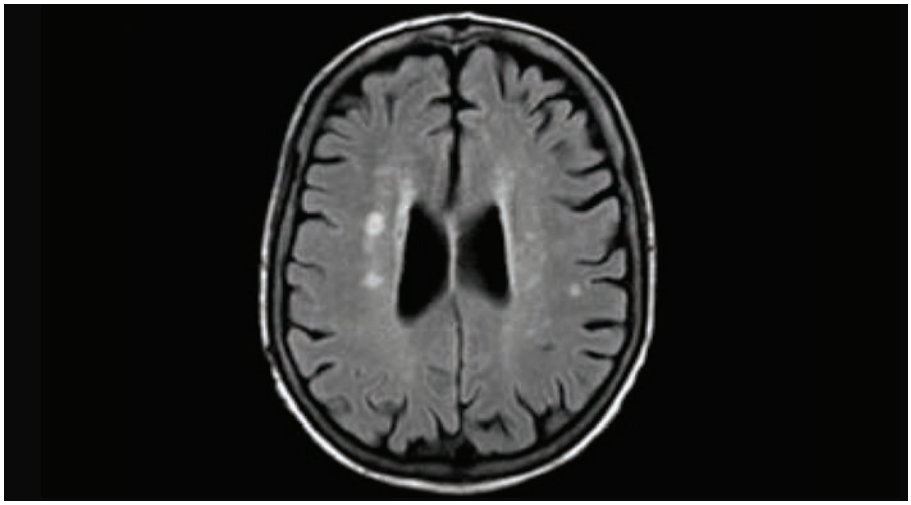
Design. Case series.

Setting. Intensive care unit.

Participants. Eight patients who underwent magnetic resonance imaging for delirium in the absence of focal neurological findings as part of their intensive care unit clinical care.

Measurements. Magnetic resonance imaging findings, clinical decisions following magnetic resonance imaging, and three-month neuropsychological outcomes were obtained.

Results. Of the eight patients, six (75%) demonstrated white matter hyperintensities, one (12%) had mild atrophy, and no patient had ischemic/hemorrhagic lesions.



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Magnetic resonance imaging did not lead to new diagnoses or immediate changes in therapy. All six patients who underwent neuropsychological testing had severe impairments in memory, executive function, and attention at three months, despite the absence of baseline cognitive impairment.

Conclusion. Magnetic resonance imaging findings in these delirious intensive care unit patients did not alter the immediate treatment course and these patients had neuropsychological impairments at three months. Future research is warranted to define the role of current and newer magnetic resonance imaging techniques in assessing and managing delirious intensive care unit patients, and to examine relationships between in-hospital magnetic resonance imaging findings (i.e. white matter hyperintensities) and short- and long-term neurological outcomes.

INTRODUCTION

Intensive care unit (ICU) delirium occurs in 60 to 80 percent of mechanically ventilated patients[1,2] and is associated with adverse outcomes.[3,4] As clinicians focus on the management of delirium,[5] uncertainty exists regarding the role of magnetic resonance imaging (MRI) in the evaluation and management of delirious ICU patients. In addition, little is currently known about neuroimaging findings in patients with delirium.[6]

Clinicians look for guidance on when brain imaging should be performed,[7] but the clinical utility of MRI in guiding in-hospital therapy in delirious ICU patients is unclear. No prior reports describe the clinical impact of MRI when ordered for delirium in the ICU. MRI may provide short-term diagnostic information (e.g., revealing stroke or abscess) to help guide therapy for delirious patients. Brain imaging may also inform long-term cognitive prognosis, which is increasingly important in light of investigations suggesting that delirious patients are at high risk for long-term cognitive impairments.[8,9] Understanding benefits of brain MRI is important as MRI has substantial costs and may expose patients to transport-related complications (e.g., arterial hypotension and hypertension, increased intracranial pressure, arrhythmias, cardiac arrest and a change in respiratory rate, hypocapnia and hypercapnia, and significant hypoxemia), an under-appreciated risk that occurs in up to 70 percent of transports.[10] Recently, Hillman et al[11] raised concerns regarding unwarranted use of high-tech neuroimaging in patients along with the related risks and costs."

In this small case series, we describe 1) the short-term clinical utility of usual care brain MRI when the primary reason for imaging was delirium of unknown etiology, excluding conditions that a clinician would deem neuroimaging appropriate and 2) describe brain MRI findings and three-month neuropsychological outcomes in the same patients.

MATERIALS AND METHODS

Patients. Patients were selected from an ongoing prospective cohort investigation of critically ill ICU patients. Inclusion criteria for this investigation were ICU admissions with shock or respiratory failure accompanied by delirium of unexplained etiology. Exclusion criteria were severe baseline cognitive impairment, anoxic brain injury, active substance abuse, life expectancy less than 24 hours, unable to obtain consent, blindness, or non-English speaking.

We collected MRI results in patients for whom MRIs were ordered by the clinical ICU team specifically for evaluation of delirium of unknown etiology (i.e., isolated delirium). We excluded patients whose MRIs were ordered for conditions for which a clinician would deem additional neuroimaging appropriate, including the following: 1) follow up of previously identified lesions (e.g., subarachnoid hemorrhage, ischemic stroke, brain abscess, and intracranial neoplasm), 2) focal neurologic deficits, 3) meningitis, 4) metastatic malignancy, 5) elevated intracranial pressure, or 6) coma.

Brain MRI. Two independent raters (Morandi, Vasilevskis) evaluated clinical records to identify primary indications for brain MRI. Clinical orders and interventions following MRI reports were recorded. In cases where raters disagreed, a third independent rater (Girard) provided additional assessments.

MRIs were performed on a 1.5-T magnet system and included FLAIR, multi-planar gradient echo T1-weighted and T-2 weighted sequences. MRI findings were recorded using radiology reports for the presence of white matter hyperintensities (WMHs), atrophy, and ischemic lesions. Severity of WMHs lesions were classified from 0 (lowest grade) to 3 (highest grade) according to a previously validated scale.[12,13]

Data collection. Demographics data, Acute Physiologic and Chronic Health Evaluation II (APACHE II) illness severity score,[14] Sequential Organ Failure Assessment (SOFA) score,[15] and comorbidities were recorded at study enrollment. Baseline cognitive abilities were assessed through surrogate interview using the validated Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE).[16] The Short IQCODE has a high reliability (Cronbach's alpha, 0.93–0.97) along with good sensitivity (75%–100%) and specificity (68%–86%) as a screening test for dementia.[16] Patients were considered cognitively intact if the total IQCODE score was less than 3.3. Delirium was assessed by clinician evaluation and with the Confusion Assessment Method for the ICU (CAM-ICU).[2,17]

Follow-up data. Three-month post-ICU discharge neuropsychological outcomes were examined using a comprehensive neuropsychological battery, which evaluated memory (i.e., Repeatable Battery for the Assessment of Neuropsychological Status delayed recall; RBANS), executive function (i.e., TRAILS B), and attention (i.e. Digits symbol in the RBANS).[18] Test

TABLE 1. MRI findings and neuropsychological scores when clinicians ordered an MRI specifically for delirium[a]

CASE	DIAGNOSIS	AGE	IQCODE SCORE[b]	COMORBIDITIES	APACHE-II SCORE[c]	SOFA SCORE[d]	CLINICAL REASON FOR IMAGING	LOS SINCE ICU ADMISSION AND DAYS OF DELIRIUM PRIOR TO MRI[e]	MRI FINDINGS: WMH, ATROPHY[f]	ORDERS FOLLOWING MRI RESULTS	FINAL REPORTED DELIRIUM DIAGNOSIS	3-MONTH FOLLOW UP[f]
1	Septic shock	43	<3.3	None	20	13	Delirium, normal CT scan	13 days of LOS, 5 days of delirium	Grade 2 No atrophy	Neurology consult, EEG and psychiatry consult	Medical delirium	Ex Func 0.1
2	Acute lung injury	75	<3.3	Diabetes, CAD COPD[g]	31	15	Agitation, normal CT	6 days of LOS, 12 days of delirium	Grade 2 No atrophy	Haloperidol, Olanzapine	Delirium due to hypoxia	Memory 32 Ex Func 0.1 Attention 16
3	ARDS	35	<3.3	None	31	15	Delirium, normal CT	9 days of LOS, 3 days of delirium	None No atrophy	Neurology consult, EEG and psychiatry consult	Delirium due to hypoxia	Memory 13 Ex Func 0.1 Attention 1
4	Septic shock	57	<3.3	None	27	14	Delirium, normal CT	7 days of LOS, 5 days of delirium	Grade 1 No atrophy	None	Delirium with negative MRI	Memory NA Ex Func 13 Attention 27
5	Acute respiratory failure due to pleural effusion	65	<3.3	Diabetes, HTN, OSA, CHF[g]	30	10	AMS, normal CT	2 days of LOS, 2 days of delirium	Grade 3 No atrophy	Neurology consult, EEG	Delirium due to hypercarbia	Patient died in the hospital
6	Septic shock	52	<3.3	HTN, CAD, HIV[g]	25	13	AMS, CT (mild atrophy)	13 days of LOS, 4 days of delirium	Grade 1 No atrophy	None	Medical delirium	Memory 42 Ex Func 13 Attention 27
7	Baclofen overdose	22	<3.3	None	15	11	AMS, normal CT	3 days of LOS, 3 days of delirium	No atrophy	Psychiatry consult	Delirium due to baclofen withdrawal	Not available
8	Septic shock	81	<3.3	None	22	13	Delirium, normal CT	2 days of LOS, 2 days of delirium	Grade 3 No atrophy	Interruption of sedationa	Medical delirium	Memory 53 Ex Func 55 Attention 58

[a]The clinical indication to perform an MRI for these patients was delirium. Patients for whom an MRI was ordered for the presence of focal neurological symptoms, ischemia at CT scan, coma, and central nervous system infections were not included in this table. All the patients included in this table were found delirious on the day of the MRI by research staff performing the CAM-ICU evaluation.

[b]The presence of cognitive impairment before hospitalization was determined via the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) at study enrollment. None of the patients included in this table had a baseline cognitive impairment (i.e., IQCODE <3.3).

[c]APACHE-II (Acute Physiology and Chronic Health Evaluation II).

[d] SOFA (Sequential Organ Failure Assessment).

[e] Length of stay (LOS), Intensive Care Unit (ICU).

[f] WMH (white matter hyperintensities) were classified from 0 to 3, based on the number and size of lesions: grade 0 (normal); grade 1 (punctiform), grade 2 (patchy or confluent), and grade 3 (diffuse) according to a previously validated scale.[12,13]

[f] NPS (Neuropsychological assessment performed at 3-month follow-up): memory (assessed with RBANS delayed call), executive functions (assessed with TRAILS B), attention (assessed with digit symbol).[18] The test scores are reported in percentile, adjusted for age, education and race based on normative databases.

[g] CAD (coronary artery disease), COPD (chronic obstructive pulmonary disease), HTN (arterial hypertension), OSA (obstructive sleep apnea), CHF (congestive heart failure), HIV (human immunodeficiency virus).

scores were adjusted for age, education, and race based on normative data.

RESULTS

Of 335 patients from the cohort, 27 received brain MRIs as a part of their clinical management in the ICU. We excluded 19 patients: coma (6), focal neurological signs (9), follow-up previous MRI (2), not delirious (1), and meningitis (1). Eight patients who received MRIs between April 2007 and January 2009 were included in our study.

Patient characteristics. Three patients had comorbidities at baseline. No patient had baseline cognitive impairment. Patient characteristics, imaging results, and outcomes are displayed in Table 1.

MRI findings. Radiology reports indicated WMHs in six patients (Table 1). Younger patients had smaller WMHs than older patients. Figure 1 shows representative MRI images for a patient with WMHs. No ischemic or hemorrhagic lesions were identified by gadopentetate dimeglumine or radiology report.

Clinical follow up to MRI. MRI did not result in new diagnoses or targeted medical/surgical therapy. WMHs and atrophy preceded new neurology or psychiatry consults and three electroencephalograms (EEG) (Table 1). The EEG showed nonspecific cerebral dysfunction (Patient 1) and no abnormalities were detected for Patients 3 and 5.

Three-month neurocognitive outcomes. Six of eight patients had corresponding three-month neuropsychological follow up. Patients had severe memory, executive function, and attention impairments (Table 1).

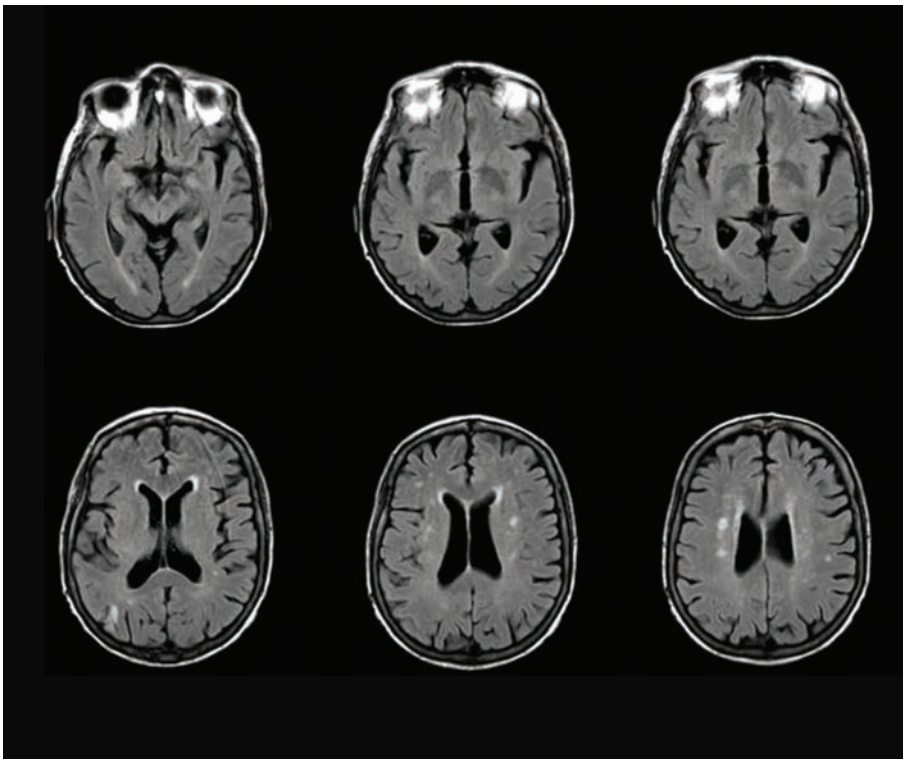

FIGURE 1. T2 FLAIR image acquired from a Phillips 1.5 scanner. Case 1 is a 43-year old woman with septic shock. Magnetic resonance imaging (MRI) was performed to evaluate delirium without focal neurologic findings following a brain computed tomograpy scan. Images are axial slices, from the top right to left and then bottom left to right, starting through the temporal lobes progressing higher in the brain through the frontal and parietal lobes. The patient did not have baseline cognitive deficits (IQCODE score <3.3). Patient exhibited no obvious subarachnoid hemorrhage, ischemic stroke, brain abscess, or intracranial neoplasm on the usual care clinical MRI. Periventricular patchy white matter lesions are seen in the lower three images. The three-month follow up neuropsychological evaluation showed severe impairment in executive function (memory and attention were not assessed as the patient was too weak to perform all tests).

DISCUSSION

The imaging findings of brain MRIs and subsequent outcomes in critically ill patients with isolated delirium are unknown. In a series of patients with isolated delirium, we found that MRIs commonly identified WMHs and brain atrophy, with more severe lesions in the elderly. MRI neuroimaging did not inform new clinical diagnoses or lead to disease-targeted treatments. Whereas results from this case series cannot rule out short-term clinical benefits of brain imaging in delirious ICU patients, our findings highlight the need to clarify the role of clinical MRI in this population.

Sparse neuroimaging data exist in delirious ICU patients. Kishi et al[19] examined 235 MRIs/computed tomograpy (CT) scans ordered as part of the clinical work-up in hospitalized, critically ill, delirious patients, recording specific lesions (i.e., subarachnoid and subdural hemorrhage and other focal lesions usually secondary to stroke). The MRI findings were considered "positive" when a medical/surgical intervention or observations in the ICU were required. The reason for ordering MRIs was unclear, and whether delirium was secondary to neural lesions is unknown. In addition, the implications of MRI in clinical decision making were not described. In our case series, we report the clinical context for ordering as well as the resulting clinical decisions. The contextual data demonstrated that clinical MRI was of limited utility for short-term medical decision making. MRI findings of WMHs did not clarify the diagnosis and lead to further neurologic testing and neuropsychiatric consultation.

Although brain MRIs in our patients did not identify specific neurologic diagnoses, imaging did reveal frequent WMHs and atrophy. WMHs in our older patients are not surprising since WMHs also occur in 5.3 percent of healthy subjects younger than 65.[20] In addition, Shioiri et al[21] found preoperative deep and white matter and thalamic abnormalities on diffusion tension imaging (DTI) were common in elderly patients with

postoperative delirium. Brain regions where white matter abnormalities occurred in areas that mediate consciousness and attention (i.e. cerebral cortices, subcortical areas), are both important features of delirium.

MRI findings in noncritically ill delirious patients are also sparse and are limited by the small sample size and population investigated. Recently, Soiza et al[6] reported two structural studies[22,23] using MRI and an additional three studies[22–24] using a mixture of MRI and CT scans. The first two studies[22,23] investigated MRI findings in patients with electroconvulsive-induced delirium and antidepressant-induced delirium, reporting frequent WMHs along with cortical atrophy and ventricular enlargement. The studies[24–26] focused on stroke patients, reporting higher proportions of individuals with brainstem, cerebellum, and caudate nucleus strokes compared to nondelirious patients.

MRI findings may have more important implications for long-term cognitive outcomes than short-term clinical decision making. WMHs are associated with neuropsychological deficits in healthy elderly patients and with poor neurological recovery in critically ill patients.[13,27] In our case series, all the patients had a different degree of WMHs and were detected with severe neuropsychological impairment at three-month follow up. Characterization of WMHs may identify patients at risk of developing long-term cognitive impairment and targets for interventions.

Our study has multiple limitations. The case-series design and the small number of patients preclude firm conclusions but bring attention to the use of clinical MRI in delirious ICU patients and future areas of research. Our population is limited to a single institution and may not generalize to other settings. The sickest patients are more likely to undergo brain imaging and therefore increase the likelihood of abnormalities. Our study does not have a control group. The selection of controls presents important challenges, as ICU nondelirious patients undergo MRI for specific clinical indications, such as ischemic-hemorrhagic lesions, hydrocephalus, abscess, and malignancy. Finally, WMHs are present in the general population, with a low prevalence in healthy individuals. WMHs may pre-date the critical illness and delirium[21,27,28] and, therefore, we cannot state causal links between delirium, MRI findings (e.g., WMHs), and cognitive outcomes. Future studies with large sample sizes including sequential brain imaging are needed, especially in light of recent published data showing that WMHs are a risk factor for delirium.[21] Researchers and clinicians should investigate other risk factors for WMHs in critically ill patients.

This case series is only a preliminary step toward understanding the impact of clinical MRI methods in identifying the etiology of isolated delirium or predicting long-term cognitive impairments. Further studies should also consider the role of advanced imaging techniques that may improve clinical decision making and prognostication. Assessment of brain perfusion using techniques such as arterial spin-labeling[29] have identified perfusion deficits not assessed by structural MRI.[30] These newer advances in clinical imaging may better identify underlying causes of delirium, allowing for targeted therapies as well as identification of patients at high risk for long-term cognitive impairments. Finally, future research should investigate the potential role of pharmacological exposure (e.g., sedatives and analgesics) on the development of WMHs.

CONCLUSIONS

The MRI findings in ICU patients with isolated delirium (i.e., unknown etiology) did not result in changes in clinical treatment. However, six of eight patients had WMHs, and the majority had severe neuropsychological impairment. This case series extends discussion regarding the acute and long-term role of assessment using MRI in critically ill patients with isolated delirium. Future research should 1) clarify the role of newly detected WMHs and 2) understand the role of current imaging techniques in the identification, treatment and long-term outcomes of delirium.

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