Things We Do for No Reason: Neuroimaging for Hospitalized Patients with Delirium

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Inspired by the ABIM Foundation's Choosing Wisely® campaign, the "Things We Do for No Reason" (TWDFNR) series reviews practices that have become common parts of hospital care but may provide little value to our patients. Practices reviewed in the TWDFNR series do not represent "black and white" conclusions or clinical practice standards but are meant as a starting place for research and active discussions among hospitalists and patients. We invite you to be part of that discussion.

CLINICAL SCENARIO

A 67-year-old woman with a history of hypertension and osteoarthritis was hospitalized for fever, flank pain, and dysuria with pyuria on urinalysis. She was diagnosed with acute pyelonephritis and started ceftriaxone, ondansetron for nausea, and oxycodone for pain. On hospital day two, she developed acute confusion that waxed and waned in severity throughout the day. On examination, she appeared mildly agitated, inattentive, and was noted to pick at her linens and garment. She was oriented to person only and had a nonfocal neurologic examination. Her nurse reported no recent falls or trauma. As part of the patient's evaluation, her attending physician ordered a head computed tomography (CT) scan.

BACKGROUND

Delirium is commonly diagnosed in hospitalized patients. It has a prevalence of 29%-64% and is associated with longer lengths of stay, higher mortality, and costs of over $164 billion per year in the United States.[1] While a number of practice guidelines have been created to help guide delirium diagnosis and management, there is not a clear consensus on when neuroimaging should be performed during the evaluation.[2-4] It should also be noted that numerous guidelines for delirium management exist, with variable quality and a heavy reliance on expert opinion.[5] Perhaps due to this lack of consensus, neuroimaging is performed in 33% to 67% of hospitalized patients with delirium.[6,7]

WHY YOU MAY THINK NEUROIMAGING IS HELPFUL IN EVALUATING UNDIFFERENTIATED HOSPITALIZED PATIENTS WITH DELIRIUM

Delirium is known to be associated with intracranial processes. For example, delirium occurs in 13% to 48% of patients with acute stroke[8] and conversely 7% of patients with new confusion evaluated in emergency departments or inpatient settings were found to have an acute stroke.[9] The inclusion of neuroimaging as part of a delirium evaluation is supported in certain circumstances, such as in patients with recent falls, focal neurologic signs (including papilledema), systemic anticoagulation,[2] or increased risk of intracranial processes such as metastatic malignancy.[4]

WHY NEUROIMAGING IS NOT HELPFUL IN EVALUATING UNDIFFERENTIATED HOSPITALIZED PATIENTS WITH DELIRIUM

A number of studies have evaluated the diagnostic yield of neuroimaging in hospitalized patients with delirium (Table).[6,7,10,11] Two studies included patients with delirium that developed after hospitalization[10,11] and two included patients with delirium at admission.[6,7]

Theisen-Toupal et al. conducted a retrospective study of 220 hospitalized general medical patients who underwent head CT scans for an indication of delirium, altered mental status, confusion, encephalopathy, somnolence or unresponsiveness.[10] Patients were excluded if they had a history of falls, head trauma, or new neurologic deficits in the preceding two weeks or if the admitting diagnosis was stroke or cerebral hemorrhage. Additionally, the authors limited patients to those who developed delirium 24 hours or more after admission. There were 6/220 (2.7%) patients identified with an acute intracranial process. Of these six patients, three were receiving anticoagulation. An additional 4/220 (1.8%) head CT scans were identified as equivocal, prompting further neuroimaging, which ultimately showed chronic findings.

Vijayakrishnan et al. performed a retrospective review of 400 hospitalized patients who underwent inpatient CT scans, then limited to those with new delirium.[11] They identified 36 patients, of which four (11%) had acute findings on CT: one case each of acute hemorrhage, subdural hematoma, brain metastases, and septic emboli. The authors state "all the four patients had preimaging clinical symptoms and signs, which warranted imaging as per guidelines suggested by the British Geriatrics Society and the Australian and New Zealand Society for Geriatric Medicine," though they do not provide further details. The strength of this paper is that it isolated patients

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TABLE. **Studies of Neuroimaging for Hospitalized Patients with Delirium**

Lead Author	Year	Study Design	Population (n)	Setting	Methods	Definition of Positive Neuroimaging	Outcome Measures	Results
Lai[6]	2010	Case Control	Adult patients admitted to a delirium unit over an 18-month period (300 patients, 200 with head CT)	Single teaching hospital in Australia	CAM used by geriatricians to identify patients. Then chart review for additional predictive risk factors. Two clinicians reviewed the clinical significance of CT results.	Intracranial abnormalities accountable for a cause of delirium that resulted in a change in patient's management.	The yield of true positive CT findings showing an intracranial cause of delirium.	29/200 (14.5%) true positive CT findings, 13 with ischemic stroke, 7 with SDH, 9 with ICH. 3/200 (1.5%) had none of the three risk factors: focal neurologic deficits, recent falls, or deterioration in consciousness.
Thiesen-Toupal[10]	2014	Retrospective Cohort	Adult patients who underwent CT head scans on multiple medical floors over a 35-month period (1,714 head CT studies, 220 scans for delirium)	Single tertiary care center in the Northeast	Indications for scans were delirium, AMS, confusion, encephalopathy, or unresponsiveness. CT scans had to be done 24 hours after admission. Patients excluded if known fall, head trauma, or new neurologic deficit in the previous two weeks or admitted diagnosis of intracranial pathology.	Defined as an intracranial process that could explain delirium. "Equivocal" scans had findings of unclear significance.	Diagnostic yield of head CT imaging for identifying the cause of non-resolving or new-onset delirium.	6/220 (2.7%) positive scans and 4/220 (1.8%) equivocal. 3/6 positive scans were in anticoagulated patients.
Vijayakrishnan[11]	2015	Retrospective Cohort	Adult hospitalized patients who had CT head scans for mental status changes over a 12-month period (400 patients, 36 with an indication of delirium)	Single tertiary care center in the Northeast	Radiology logs reviewed using keywords: confusion, delirium, agitation, and AMS. Charts reviewed to include patients who developed AMS while inpatient. Patients with long-standing AMS with no worsening during inpatient stay were excluded.	Acute changes: new stroke, hemorrhage, infection, or neoplasm.	Acute CT scan findings that altered management.	4/36 (11%) CT scans with acute changes in patients with inpatient delirium. All 4 met imaging guidelines for recent falls, new neurologic deficits. or anticoagulation.
Hijazi[7]	2015	Retrospective Cohort	Adult patients diagnosed with delirium either at or during admission over a 20-month period (1653 patients with delirium, 538 with CT and/or MRI imaging)	Single tertiary care center in Australia	Patients selected by using ICD-10 codes for delirium or disorientation, disorientation NOS, other delirium, and delirium NOS. Delirium must have been documented prior to imaging request.	Acute/subacute stroke, hemorrhage, abscess, neoplasm, vasculitis, PRES, encephalitis, acute demyelination, or fat embolism.	The yield of CT and/or MRI imaging in patients with possible delirium.	78/538 (14.5%) positive CT head or MRI brain scans. Patient exam findings or risk factors for intracranial processes not described.

Abbreviations: AMS, altered mental status; CAM, Confusional Assessment Method; CT, computed tomography; ICH, intracerebral hemorrhage; MRI, magnetic resonance imaging; NOS, not otherwise specified; PRES, posterior reversible encephalopathy, syndrome; SAH, subarachnoid hemorrhage; SDH, subdural hemorrhage.

who developed delirium while hospitalized; however, conclusions were limited by the small sample size.

Lai et al.'s case-control study evaluated 300 consecutive patients admitted to a delirium unit over 18 months.[6] Of these 300 patients, 200 (67%) had CT performed; 29/200 (14.5%) had intracranial findings on CT that explained their delirium, including 13 ischemic strokes, seven subdural hemorrhages, nine intracerebral hemorrhages, and three additional ischemic strokes that evolved on follow-up imaging but were not present on the initial scans. The authors performed univariate and multivariate analyses to identify risk factors for an intracranial cause of delirium. Only 3/29 patients with a positive scan did not have one of three main risk factors the authors identified: a fall in the preceding two weeks, new neurologic findings, or sudden deterioration of consciousness. It should be noted that authors did not define "deterioration of consciousness" and that all patients had confusion on admission to the unit, rather than developing during hospitalization.

Hijazi et al. conducted a retrospective cohort study over a 20-month period of 1,653 patients with delirium at the time of admission or during their hospitalization. Patients with delirium due to drug or medication withdrawal or "psychiatric reasons" were excluded. Overall, 538 (32.5%) patients underwent CT, MRI or both, and 78 (14.5%) patients had a positive finding on neuroimaging. This study's 14.5 % overall yield matches that of Lai et al. Unfortunately, the study included all patients with delirium and did not report the rates of fall, neurologic deficits, and/or use of anticoagulation among those with positive neuroimaging. This limits the generalizability of the findings to a cohort of patients without intracranial pathology risk factors.

The reported yield of neuroimaging for hospitalized patients with delirium ranged from 2.7% to 14.5% across studies. However, in studies taking into account specific patient risk factors; the reported yields in patients without focal neurologic findings, new decline in mental status, systemic anticoagulation, or recent falls were 0%,[11] 1.4%,[10] and 1.5%.[6] While a rate of 1.5% may appear high for a serious outcome such as stroke or intracranial bleeding, it is comparable to rates reported for missed major cardiac events in clinical algorithms for evaluating chest pain.[12] It should also be noted that neuroimaging is imperfect

for acute stroke, and thus the positive or negative predictive value may be poor in the setting of low prevalence. For example, for detection of any acute stroke, the sensitivity/specificity of MRI and CT are 83%/97% and 26%/98% respectively.[13]

Neuroimaging is expensive and has risks. The average charge for a head CT is approximately $1,400 at academic institutions.[14] Moreover, computed tomography exposes patients to significant radiation and up to 2% of malignancies in the United States may be attributable to prior tomography exposure.[15] Additionally, there are non-negligible rates of incidental findings during neuroimaging, 1% for CT[16] and 2.7%-13.7% for MRI,[17,18] which may result in further evaluation or treatment that causes significant patient anxiety. Obtaining neuroimaging on delirious patients can be time consuming and labor intensive, which could delay care to other patients. Additionally, sedating medications are often administered to agitated patients prior to imaging, which risk worsening delirium. Ordering neuroimaging for all patients with acute delirium, therefore, exposes the large majority to unnecessary costs and potential harms.

WHEN NEUROIMAGING TO EVALUATE DELIRIUM IN HOSPITALIZED PATIENTS COULD BE REASONABLE

The diagnostic yield of head CT in the evaluation of delirium is significantly higher in patients with specific risk factors. Lai et al. found adjusted odds ratios for abnormal CT of 18.2 in patients with new focal deficits, 5.6 with a fall in the preceding two weeks and 4.6 in patients with deterioration in consciousness. Patients with systemic anticoagulation had higher unadjusted, (OR 2.4) though not adjusted odds of having an abnormal CT.[6] Thiesen-Toupal et al. excluded patients with recent falls or neurologic deficits but reported that three out of six delirious patients with abnormal neuroimaging were anticoagulated.[10] Vijayakrishnan et al. found that all four delirious patients with intracranial findings met guideline criteria for neuroimaging.[11] Thus, current recommendations for neuroimaging in delirious patients with falls, focal neurologic deficits, or systemic anticoagulation are appropriate. In situations when a provider lacks an accurate history and is unable to determine if risk factors are present (for example a confused patient found sitting on the floor next to the bed), it may also be reasonable to consider neuroimaging.

Data are limited, but some authors advocate for neuroimaging in cases of delirium that do not improve with treatment.[6] Additionally, it may be reasonable to consider neuroimaging in delirium patients with predispositions to embolic or metastatic intracranial processes such as endovascular infections and certain malignancies.[4]

WHAT YOU SHOULD DO INSTEAD OF NEUROIMAGING TO EVALUATE DELIRIUM IN HOSPITALIZED PATIENTS

Hospitalized patients with acute confusion should be assessed for delirium with a validated instrument such as the Confusion Assessment Method (CAM).[19,20] The original CAM included several components: acute change in mental status with a fluctuating course and inattention, plus either disorganized thinking and/or altered level of consciousness. Multiple delirium assessment tools have been created and validated, all of which include inattention as a required feature. A recent hospital-based study using a two-item bedside test asking the patient to name the day of the week and list the months of the year backwards detected delirium with a sensitivity of 93% and specificity of 64%.[21] Once the diagnosis of delirium is established, evaluation should begin with a careful history and physical examination focused on the identification of risk factors such as physical restraints, indwelling urinary catheters, and drugs known to precipitate delirium, particularly those with withdrawal potential, anticholinergic properties, and sedative-hypnotic agents.[22-24] Delirium may be the first harbinger of serious medical illness and specific testing should be guided by clinical suspicion. In general, a thorough physical examination should look for focal neurologic deficits, hypoxia, signs of infection, and other inflammatory or painful processes that could precipitate delirium.[25] Targeted laboratory evaluation may include a basic metabolic panel to identify electrolyte (including calcium) and metabolic derangements, complete blood count, and urinalysis if infection is suspected.

RECOMMENDATIONS

- Use a validated instrument such as CAM to evaluate hospitalized patients who develop altered mental status.
- Delirious patients should undergo a thorough history including a review of medications, physical exam, and targeted laboratory testing aimed at identifying common risk factors and precipitants of delirium that should be addressed.
- Perform neuroimaging if there is a history of fall or head trauma in the preceding two weeks, any new focal abnormalities on neurologic exam or if the patient is receiving systemic anticoagulation.
- It may be reasonable to consider neuroimaging for patients with an atypical course of delirium, such as a sudden decline in the level of consciousness, persistence despite addressing identified factors, or if there is a high degree of suspicion for embolic or metastatic processes.

CONCLUSIONS

Performing neuroimaging in undifferentiated patients who develop delirium while hospitalized has a low diagnostic yield, is costly, and is potentially harmful. Neuroimaging should be reserved for those with identified risk factors for intracranial pathology. For the patient described in the initial vignette with no risk factors for intracranial cause, neuroimaging would be unlikely to contribute to her care. To change provider beliefs and behaviors regarding neuroimaging, prospective studies evaluating guideline implementation are needed. However, based on the current evidence, neuroimaging should be reserved for those with identified risk factors.

Do you think this is a low-value practice? Is this truly a "Thing We Do for No Reason?" Share what you do in your practice and join in the conversation online by retweeting it on Twitter

(#TWDFNR) and liking it on Facebook. We invite you to propose ideas for other "Things We Do for No Reason" topics by e-mailing TWDFNR@hospitalmedicine.org.

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References

1. Inouye SK, Westendorp RG, Saczynski JS. Delirium in elderly people. *Lancet*. 2014;383(9920):911-922. doi: 10.1016/S0140-6736(13)60688-1.
2. Clinical practice guidelines for the management of delirium in older people. 2006; https://www2.health.vic.gov.au/Api/downloadmedia/%7BDAA8404B-FEE7-4BDA-8A1E-A32494783B7F%7D. Accessed June 4, 2018.
3. Delirium: prevention, diagnosis and management. *NICE Guidance* 2010; https://www.nice.org.uk/guidance/cg103. Accessed June 4, 2018.
4. Michaud L, Bula C, Berney A, et al. Delirium: guidelines for general hospitals. *J Psychosom Res*. 2007;62(3):371-383. doi: 10.1016/j.jpsychores.2006.10.004.
5. Bush SH, Marchington KL, Agar M, Davis DH, Sikora L, Tsang TW. Quality of clinical practice guidelines in delirium: a systematic appraisal. *BMJ Open*. 2017;7(3):e013809. doi: 10.1136/bmjopen-2016-013809.
6. Lai MM, Wong Tin Niam DM. Intracranial cause of delirium: computed tomography yield and predictive factors. *Intern Med J*. 2012;42(4):422-427. doi: 10.1111/j.1445-5994.2010.02400.x.
7. Hijazi Z, Lange P, Watson R, Maier AB. The use of cerebral imaging for investigating delirium aetiology. *Eur J Intern Med*. 2018;52:35-39. doi: 10.1016/j.ejim.2018.01.024.
8. Oldenbeuving AW, de Kort PL, Jansen BP, Roks G, Kappelle LJ. Delirium in acute stroke: a review. *Int J Stroke*. 2007;2(4):270-275. doi: 10.1111/j.1747-4949.2007.00163.x.
9. Benbadis SR, Sila CA, Cristea RL. Mental status changes and stroke. *J Stroke Cerebrovasc Dis*. 1994;4(4):216-219. doi: 10.1016/S1052-3057(10)80093-X.
10. Theisen-Toupal J, Breu AC, Mattison ML, Arnaout R. Diagnostic yield of head computed tomography for the hospitalized medical patient with delirium. *J Hosp Med*. 2014;9(8):497-501. doi: 10.1002/jhm.2198.
11. Vijayakrishnan R, Ramasubramanian A, Dhand S. Utility of head CT scan for acute inpatient delirium. *Hosp Top*. 2015;93(1):9-12. doi: 10.1080/00185868.2015.1012928.
12. Backus BE, Six AJ, Kelder JC, et al. A prospective validation of the HEART score for chest pain patients at the emergency department. *Int J Cardiol*. 2013;168(3):2153-2158. doi: 10.1016/j.ijcard.2013.01.255.
13. Chalela JA, Kidwell CS, Nentwich LM, et al. Magnetic resonance imaging and computed tomography in emergency assessment of patients with suspected acute stroke: a prospective comparison. *Lancet*. 2007;369(9558):293-298. doi: 10.1016/S0140-6736(07)60151-2.
14. Paul AB, Oklu R, Saini S, Prabhakar AM. How much is that head CT? Price transparency and variability in radiology. *J Am Coll Radiol*. 2015;12(5):453-457. doi: 10.1016/j.jacr.2014.12.016.
15. Brenner DJ, Hall EJ. Computed tomography--an increasing source of radiation exposure. *N Engl J Med*. 2007;357(22):2277-2284. doi: 10.1056/NEJMra072149.
16. Eskandary H, Sabbagh M, Khajehpour F, Eskandari M. Incidental findings in brain computed tomography scans of 3000 head trauma patients. *Surg Neurol*. 2005;63(6):550-553; discussion 553. doi: 10.1016/j.surneu.2004.07.049.
17. Vernooij MW, Ikram MA, Tanghe HL, et al. Incidental findings on brain MRI in the general population. *N Engl J Med*. 2007;357(18):1821-1828. doi: 10.1056/NEJMoa070972.
18. Morris Z, Whiteley WN, Longstreth WT, Jr., et al. Incidental findings on brain magnetic resonance imaging: systematic review and meta-analysis. *BMJ*. 2009;339:b3016. doi: 10.1136/bmj.b3016.
19. Inouye SK, van Dyck CH, Alessi CA, Balkin S, Siegal AP, Horwitz RI. Clarifying confusion: the confusion assessment method. A new method for detection of delirium. *Ann Intern Med*. 1990;113(12):941-948. doi: 10.7326/0003-4819-113-12-941.
20. Wei LA, Fearing MA, Sternberg EJ, Inouye SK. The Confusion Assessment Method: a systematic review of current usage. *J Am Geriatr Soc*. 2008;56(5):823-830. doi: 10.1111/j.1532-5415.2008.01674.x.
21. Fick DM, Inouye SK, Guess J, et al. Preliminary development of an ultrabrief two-item bedside test for delirium. *J Hosp Med*. 2015;10(10):645-650. doi: 10.1002/jhm.2418.
22. Tune L, Carr S, Hoag E, Cooper T. Anticholinergic effects of drugs commonly prescribed for the elderly: potential means for assessing the risk of delirium. *Am J Psychiatry*. 1992;149(10):1393-1394. doi: 10.1176/ajp.149.10.1393.
23. Inouye SK, Schlesinger MJ, Lydon TJ. Delirium: a symptom of how hospital care is failing older persons and a window to improve the quality of hospital care. *Am J Med*. 1999;106(5):565-573. doi: 0.1016/S0002-9343(99)00070-4.
24. Marcantonio ER. Delirium in hospitalized older adults. *N Engl J Med*. 2017;377(15):1456-1466. doi: 10.1056/NEJMc1714932.
25. Inouye SK, Charpentier PA. Precipitating factors for delirium in hospitalized elderly persons. Predictive model and interrelationship with baseline vulnerability. *JAMA*. 1996;275(11):852-857. doi: 10.1001/jama.1996.03530350034031.