

Are Intracranial Extravascular Calcifications and Ventricular Communicating Hydrocephalus Correlated with Delirium in Veterans at a Veterans Affairs Hospital

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Abstract

Background: The role of anatomic pathology in delirium is not fully understood. Computed tomography (CT) is an economic modality to screen the elderly in the ER or on hospital admission for anatomic variations associated with delirium risk.

Objectives: To assess the relation of intracranial extravascular calcifications and ventricular communicating hydrocephalus with delirium in hospitalized veterans.

Design: Case control retrospective chart review.

Setting: United States Veterans Affairs Medical Center.

Participants: Hospitalized veterans with (no. 100) and without (no. 100) delirium that were matched for age, gender and race.

Intervention: Computed tomography (CT) examination by a radiologist blinded to diagnoses of veterans.

Measurements: Presence or absence of intracranial extravascular calcifications globally and in the basal ganglia, frontal, temporal, parietal, and occipital lobes and the cerebellum, in addition to the presence or absence of ventricular communicating hydrocephalus.

Results: There were no differences between groups of hospitalized veterans with delirium and without delirium for intracranial extravascular calcifications globally or by anatomical site, nor for the presence of ventricular communicating hydrocephalus.

Conclusions: Based on current literature, intracranial extravascular calcifications and ventricular communicating hydrocephalus were hypothesized to alter brain reserve and thus be more present in hospitalized veterans with delirium, compared to hospitalized veterans without delirium. These hypotheses were not supported in these preliminary results as assessed by CT scans. Continuing studies are needed to clarify the role of cranial anatomical variations as validated indices for delirium in veterans and the general population.

Keywords: Delirium; Ventricular Intracranial Extravascular Calcifications; Communicating Hydrocephalus; Veterans; Computed Tomography

Introduction

Delirium is a disorder of attention and concentration most often associated with the elderly. The risk of delirium increases in elderly hospitalized patients, with prevalence as high as 56 percent in some cases. The mortality rates ranging from delirium range 25 - 33 percent [1]. Studies have demonstrated that 32 to 96 percent of elderly patients with delirium were discharged from a hospital with ongoing delirium symptoms [2]. Moreover, in some cases, delirium is not resolved at hospital discharge and the subsequent length and severity of post-discharge delirium continues to diminish brain reserve with progressive cognitive deficits [3]. Delirium in older hospitalized patients is of particular concern as patients aged 65 years and older currently account for more than 48 percent of total hospital care days [4]. The development of delirium has been associated with increased functional decline, caregiver burden, persistent functional decline, increased nursing time per patient, higher per day hospital costs, increased length of hospital stay, higher rates of nursing home placement, and increased morbidity and mortality [5].

Intracranial extravascular calcifications

Intracranial extravascular calcifications are the most common head computed tomography (CT) finding and are associated with aging, disease and traumatic brain injury (TBI) [6,7]. In aging, physiologic or benign calcifications can often be found in many parts of the brain, such as the basal ganglia, choroid plexus, and cerebellum. Congenital disorders such as neurofibromatosis, tuberous sclerosis, and Sturge-Weber syndrome are also associated with intracranial calcifications. In addition, central nervous system infections such as cytomegalovirus (CMV), toxoplasmosis, human immunodeficiency virus (HIV), herpes virus, cysticercosis, tuberculosis, cryptococcosis demonstrate associations with intracranial calcifications on imaging [6]. Furthermore, the presence and volume of coronary artery calcifications are reported to be associated with advanced age and male gender, as well as independently associated with cardiovascular risk factors [8]. Subedi, *et al.* have reported that visual scoring of intracranial internal carotid calcifications employing non-contrast cranial computed tomographic scans, has “excellent observer agreements”, suggesting that visual intracranial internal carotid artery scores could be a rapid and practical method for epidemiological studies [9]. There is no current consensus as to whether the neuropathogenesis related to the volume of intracranial extravascular calcifications is related to delirium.

Veterans are a unique population and have multiple risk factors for intracranial extravascular calcifications secondary to military duty activities. Dystrophic calcifications occur as a result of chronic sequelae from ischemia, trauma, surgery and radiation therapy. In the case of veterans, especially combat veterans, posttraumatic calcifications can be imaged in the capsules surrounding subdural and epidural hematomas [6]. Combat stress and long deployments are associated with a time related continuum of psychiatric disorders such as post-traumatic stress disorder (PTSD), anxiety and depression [10-13]. A significant number of veterans seen in Veterans Affairs (VA) medical centers have been involved in high risk training and deployments that increased their risk of brain pathology from both head and body trauma, in addition to significant psychological stressors with compromised mental health [11,14,15].

Studies indicate that “emergence delirium” in combat veterans undergoing non-intubated surgery is related to multiple factors, including age (< 40 years, > 64 years), anesthesia with etomidate, premedication with benzodiazepines, and higher postoperative pain scores [16]. Other factors contributing to combat veterans’ post-surgical emergence delirium are concurrent physiologic (86.8%) and psychological (97.1%) factors. In this population, post-surgical delirium is associated with traumatic brain injury (54.2%), PTSD (88%) and anxiety (84.8%) [13]. A study was conducted of the pathology recorded in Iraq and Afghanistan soldiers, as reported at a US Army Warrior Transition Center [11,13]. Of 120 active duty US Army soldiers, 90 percent had chronic pain in addition to medical and mental health comorbidities. Of these, 44 percent were recovering from trauma and/or surgery, 75 percent had chronic pain and 12 percent were diagnosed with traumatic brain injuries. Twenty-two percent of the soldiers demonstrated cognitive pathology most probably related to concurrent anxiety disorders, mood disorders, traumatic brain injuries, headaches and seizures [11]. Combat veterans have a higher prevalence of delirium compared to non-combat persons [16,17].

Ventricular communicating hydrocephalus

Communicating hydrocephalus, commonly referred to as normal-pressure hydrocephalus, occurs when there is unobstructed communication between the ventricles and subarachnoid space. It is most often caused by defective absorption of cerebrospinal fluid (CSF) and less often with insufficient venous drainage or CSF overproduction. Hydrocephalus often has a delayed onset and can easily be misdiagnosed as dementia or other age related diseases. Communicating hydrocephalus is thought to have multiple etiologies including, but limited to, intraventricular hemorrhage, meningitis, TBI and subarachnoid hemorrhage [18]. According to the Hydrocephalus Association, an estimated 294,000 service members who have sustained a TBI during deployment of Iraqi and Afghanistan, at least 30,000 (10.1%) are expected to develop hydrocephalus [18]. In contrast, the prevalence of communicating hydrocephalus is estimated to be 0.5 percent of the general population 65 years or older. However, this is likely an underestimate due to lack of recognition by patients and physicians unfamiliar with this condition [19].

It follows that many veterans who had combat deployments, at least throughout modern history, have an increased risk factor for hydrocephalus. Thus, veterans from WWII, the Korean War, the Vietnam War, the Persian Gulf War and the Iraq and Afghanistan campaigns, in addition to many other combat military excursions, have a higher risk of communicating hydrocephalus than non-veterans. A 2009 Pentagon study of soldiers recovering from combat theater tours revealed that they would memorize answers on parts of the Military Acute Concussion Evaluation screening in order to stay in theater or to return for additional combat tours. The Pentagon also reported that the annual prevalence of brain injuries in the military increased from 23,217 in 2007 to 32,625 in 2011 secondary to improved screening and evaluation protocols. Consequently, the House Appropriations Committee recommended that the Department of Defense increase its investments in hydrocephalus research [18].

The role of brain reserve in the context of delirium

Brain reserve is dynamic and changes with aging and disease [20]. Reserve is related to the level of structural alterations of brain along a continuum from healthy to severely impaired, such as in end stage dementia [21,22]. Research demonstrates that some individuals demonstrate less cognitive impairment than others with comparable brain injury or neuropathology [23,24]. Also, as the susceptibility of delirium's acute decline of cognition and attention varies between individuals [22], the relationship of brain reserve in the context of delirium is the subject of ongoing investigation [22,25]. There are no validated measures of neuropathology in delirium and thus the neuropathological basis of delirium is poorly understood [22]. As delirium has a multifactorial etiology and promotes poor outcomes regardless of the cause when controlling for underlying factors [22], an important clinical question concerns the contribution of preexisting neuropathology such as intracranial extravascular calcifications and ventricular communicating hydrocephalus to delirium onset in similar populations. More specifically, can intracranial extravascular calcifications and ventricular communicating hydrocephalus, which may alter brain reserve, be measures of risk for delirium? It has, however, been suggested that delirium outcomes may be attributable to the presence of the delirium itself, and not simply to the underlying neuroanatomical pathology that may alter brain reserve [1,22,26,27].

Aim of the Study

The aim of this study was to investigate possible associations between underlying neuroanatomical pathology and delirium, specifically with regard to intracranial extravascular calcifications and ventricular communicating hydrocephalus.

Study Hypotheses

Based on the incidence of trauma related brain injuries in soldiers and veterans, it can be postulated that these anatomical brain deficits eventually may reduce anatomical reserve for veterans and the elderly with increased delirium risk. Combat veterans have an increased risk of postsurgical delirium, intracranial extravascular calcifications and ventricular communicating hydrocephalus. This paper's research neuroradiologist hypothesized that the neuroanatomical abnormalities of intracranial extravascular calcifications and ventricular communicating hydrocephalus may be more frequently viewed on head CT scans of predominantly aging hospitalized veterans with delirium when compared to veterans without delirium. Two null hypotheses were examined: 1) intracranial calcifications are not associated with delirium; and 2) ventricular communicating hydrocephalus is not associated with delirium.

Methods

Study population

This retrospective study was approved by the Veterans Affairs (VA) Institutional Review Board and the VA Research Committee. Veterans with delirium (no. 100) and without delirium (no. 100) were selected in a case control retrospective chart review from the VA data base that had a head CT associated with their inpatient hospitalization. For veterans who were diagnosed with delirium on multiple admissions, the first admission visit accompanied with a head CT was chosen. Both groups were pre-screened utilizing DSM IV-TR criteria to verify the existence or absence of delirium in their respective matched groups. Veterans who had ICD-9 diagnoses of delirium, but no independent evaluation of its presence, were removed from consideration.

Head CTs

The head CT scans of each patient with and without delirium were examined for intracranial extravascular calcifications, and communicating hydrocephalus. Intracranial extravascular calcifications were graded as present or not present in the basal ganglia, frontal, temporal, parietal, and occipital lobes and the cerebellum. They were also assessed as “generalized” which included a comparison of all anatomical areas of the brain in each veteran in the delirium group compared to the non-delirium group. Communicating hydrocephalus was assessed as present or not present. To provide grading uniformity, all the head CT readings were performed by the same neuroradiologist. The radiologist was blinded to the veterans’ demographics and medical history.

Data analysis

To examine the statistical association of intracranial extravascular calcifications and ventricular communicating hydrocephalus with delirium in hospitalized veterans, a chi-square test was performed for each of the categorical variables with a p-value equal to or less than 0.05 considered significant. No adjustment for multiple statistical tests was attempted because this observational study is exploratory and hypothesis-generating [28].

Results

Intracranial extravascular calcifications

No difference was found between the veterans with and without delirium regarding intracranial extravascular calcifications, either globally (generalized), or when examined by specific anatomical site: basal ganglia, frontal lobe, temporal lobe, parietal lobe, occipital lobe and cerebellum (Table 1). Only one subject in the control group and delirium groups respectively had calcification in the cerebellum, and only one subject in the delirium group had calcifications globally. No other subjects had notable calcifications except in the basal ganglia, where the difference was non-significant ($\chi^2 = .01$, $df = 1$, $p = 0.8$).

Intracranial Extravascular Calcifications	P value
Generalized	0.992
Basal Ganglia	0.767
Frontal	*
Temporal	*
Parietal	*
Occipital	*
Cerebellar	0.992
Communicating Hydrocephalus Ventricular	
More Prominent than Sulci	0.149
Less Prominent than Sulci	0.421

Table 1: Association of extravascular calcifications and communicating hydrocephalus ventricular in veterans with and without delirium. *: Calcifications not present.

Ventricular communicating hydrocephalus

There was no significant difference between the delirium and non-delirium groups when examined for the presence or absence of ventricular communicating hydrocephalus (Table 2).

Lesion Sites	p-value	Odds ratio
Atrophy		
Generalized	0.6142	1.31
Frontal	0.8604	1.25
Temporal	0.2230	4.13
Parietal	0.0438	8.70
Cerebellar	0.0406	**
Communicating Hydrocephalus Ventricular		
More Prominent than Sulci	.3088	0.15
Less Prominent than Sulci	.4210	0.42

Table 2: Association of atrophy and communicating hydrocephalus in veterans with and without delirium.

***: Cannot be computed because only delirium subjects (n = 6) have cerebellar atrophy.*

Discussion

The risk of delirium may be attributed to the coalescence of multiple factors including preexisting neuroanatomical changes with diminished brain reserve and even potential environmental stressors such as pathologically sustained high cortisol levels observed during stress and fatigue combined with a concurrent progressing disease processes.

Role of intracranial extravascular calcifications in delirium

In the current study, it was hypothesized that the null hypothesis would be rejected given the relationship of intracranial extravascular calcifications with aging, disease and TBI [6,7]. It was expected that the alternative hypothesis would be verified by imaging a significantly greater diffuse brain intracranial extravascular calcifications from disease and past head trauma in the hospitalized veteran population with delirium when compared to age, gender and raced matched veterans without delirium. In addition, it was predicated that there would be more intracranial extravascular calcifications on head CT in a higher number of specific brain areas (i.e. basal ganglia; frontal lobe; temporal lobe; parietal lobe; occipital lobe; and cerebellum) in veterans with delirium compared to those without delirium.

In this study, the alternative hypotheses of finding more generalized and localized intracranial extravascular calcifications on head CT were rejected as there were no significant differences between the veterans with and without delirium. This result was unexpected given that extravascular calcifications alter brain reserve and thus potentially a lower threshold for delirium onset [6]. Intracranial extravascular calcifications are one of the most common findings with aging and disease. For example, it has been estimated that approximately forty percent of healthy persons have intracranial calcifications in the pineal gland by 20 years of age [29]. Also, increasing age is associated with increased risk of infections, congenital disorders and metabolic disorders which may also alter brain reserve. Moreover, intracranial extravascular calcifications are also found in some combat veterans that often have posttraumatic calcifications in the capsules surrounding the subdura on head CT [6]. To the best of our knowledge, the role of intracranial extravascular calcifications in delirium has not been described in the general population or in veterans when examining the number and/or site of these abnormalities. Despite associations

with trauma and disease comorbidities with neurogenesis such as intracranial extravascular calcifications, Makariou and Patsalides did suggest that the slow evolution of intra- and extra-cranial calcifications are not an independent risk factor for delirium [6]. However, Makariou and Patsalides did suggest that the slow evolution of intracranial calcifications could make them a dependent risk factor for delirium [6]. This hypothesis was not supported by the current study findings.

Role of ventricular communicating hydrocephalus in delirium

Ventricular communicating hydrocephalus resulting from brain trauma is a variant of posttraumatic hydrocephalus (PTH) [30]. There is full communication between the ventricles and the subarachnoid space in communicating hydrocephalus. The differential diagnosis including PTH, cerebral atrophy and ventricular enlargement is fundamental for prognosis and treatment. If PTH goes unrecognized or untreated, post TBI morbidity and mortality is increased [31,32]. Although incidence varies among studies, in part due to different criteria for posttraumatic hydrocephalus (PTH) diagnosis, it is a frequent and serious complication following a TBI [33-35].

The null hypothesis in the current study was that there would be no difference in the frequency of ventricular communicating hydrocephalus on head CT between veteran groups with and without delirium. However, it was expected that the alternative hypothesis would be confirmed given the veterans' risk of exposure to PTH when extrapolating from the studies relating the risk Iraqi and Afghanistan soldiers and veterans with TBI developing hydrocephalus [18]. Accepting the alternative hypothesis was also based on extrapolation from the general medical and psychiatric history of today's active duty soldiers [11,13] and to the older Vietnam veteran population. It is known that a significant number of recent and older veterans seen in the VA have been involved in high risk training and deployments that have increased their risk of brain pathology from both head and body trauma in addition to significant psychological stressors with compromised mental health [14]. Hence, the association of training and combat related head traumas was hypothesized to make ventricular communicating hydrocephalus a more common head CT finding in the delirious veteran group. In this study, however, no significant differences in ventricular communicating hydrocephalus were found between veterans with and without delirium.

Particularly in the elderly, delirium commonly leads to altered brain reserve accompanied by decreased quality of life. The sequelae of delirium are often not or only partially reversible. One of the major goals of geriatric researchers is to investigate the multifactorial etiology of delirium in the attempt to find validated measures of neuropathology in delirium risk. Such validated measures, e.g. common CT signs of altered brain reserve, would aid in reducing the number, duration and severity of delirium at hospital intake, during hospitalization and following discharge. In addition to assessing delirium risk, validated delirium risk indices should improve delirious elder veterans and non-veterans post-discharge outcomes. This study's findings suggest that intracranial extravascular calcifications and ventricular communicating hydrocephalus in elderly hospitalized veterans may not be associated with an elevated risk of delirium. Continuing efforts are needed to clarify whether intracranial extravascular calcifications and ventricular communicating hydrocephalus and other anatomic pathologies in delirium can be used as validated delirium risk factors.

Disclaimer

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Bibliography

1. Inouye SK., *et al.* "Delirium: A symptom of how hospital care is failing older persons and a window to improve quality of hospital care". *The American Journal of Medicine* 106 (1999): 565-573.
2. Saravay SM., *et al.* "How do delirium and dementia increase length of stay of elderly general medical inpatients?" *Psychosomatics* 45 (2004): 235-242.

3. Kakuma R, *et al.* "Delirium in older emergency department patients discharged home: effect on survival". *Journal of the American Geriatrics Society* 51 (2003): 443-450.
4. A Profile of Older Americans: 2001. Administration on Aging, U.S. Department of Health and Human Services Washington, DC. Is this right with the 2002 (2001).
5. Leslie DL, *et al.* "Consequences of preventing delirium in hospitalized older adults on nursing home costs". *Journal of the American Geriatrics Society* 53 (2005a): 405-409.
6. Makariou E and Patsalides AD. "Intracranial calcifications". *Applied Radiology* 38.11 (2009): 48-60.
7. Lehto LJ, *et al.* "Detection of Calcifications In Vivo and Ex Vivo After Brain Injury in Rat Using SWIFT". *Neuroimage* 61.4 (2012): 761-772.
8. de Weert TT, *et al.* "Intracranial Internal Carotid Artery Calcifications: Association with Vascular Risk Factors and Ischemic Cerebrovascular Disease". *American Journal of Neuroradiology* 30 (2009): 177-184.
9. Subedi D, *et al.* "Intracranial Carotid Calcification on Cranial Computed Tomography. Visual Scoring Methods, Semiautomated Scores, and Volume Measurements in Patients With Stroke". *Stroke* 46.9 (2015): 2504-2509.
10. McGuire JM and Burkard JF. "Risk factors for emergence delirium in U.S. military members". *Journal of Peri Anesthesia Nursing* 25 (2010): 392-401.
11. Detweiler MB, *et al.* "VAMC-US Army Fort Bragg Warrior Transition Clinic Tele-Psychiatry Collaboration: 12- Month Clinic Prospective". *Telemedicine and e-Health* 18 (2012): 81-86.
12. McGuire JM. "The incidence of and risk factors for emergence delirium in U.S. military combat veterans". *Journal of Peri Anesthesia Nursing* 27 (2012): 236-245.
13. Wilson JT. "Pharmacologic, Physiologic, and Psychological Characteristics Associated with Emergence Delirium in Combat Veterans". *AANA Journal* 82.5 (2014): 355-362.
14. Litz B and Orsillo SM. "Iraq War Clinician Guide". Department of Veterans Affairs, National Center for PTSD. Chapter 3, The Returning Veteran of the Iraq War: Background Issues and Assessment Guidelines (2015).
15. J Rehabil Res Dev. "VA/DoD Clinical Practice Guideline for Management of Concussion/Mild Traumatic Brain Injury". Management of Concussion/mTBI Working Group 46.6 (2009): CP1-68.
16. Radtke FM, *et al.* "Risk factors for inadequate emergence after anesthesia: emergence delirium and hypoactive emergence". *Minerva Anesthesia* 76.6 (2010): 394-403.
17. Yu D, *et al.* "Emergence agitation in adults: risk factors in 2,000 patients". *Canadian Journal of Anesthesia* 57.9 (2010): 843-848.
18. Hydrocephalus Fact Sheet. National Institute of Neurological Disorders and Stroke (2015).
19. Hydrocephalus. Columbia Neurosurgeons, Department of Neurosurgery (2015).
20. Sachdev PS and Valenzuela M. "Brain and cognitive reserve". *American Journal of Geriatric Psychiatry* 17.3 (2009): 175.
21. Stern Y. "Cognitive reserve". *Neuropsychologia* 47.10 (2009): 2015-2028.
22. Jones RN, *et al.* "Aging, brain disease, and reserve: implications for delirium". *The American Journal of Geriatric Psychiatry* 18.2 (2010): 117-127.

23. Blessed G., *et al.* "The association between quantitative measures of dementia and of senile change in the cerebral grey matter of elderly subjects". *British Journal of Psychiatry* 114.512 (1968): 797-811.
24. Satz P. "Brain reserve capacity on symptom onset after brain injury: A formulation and review of evidence for threshold theory". *Neuropsychology* 7.3 (1993): 273-295.
25. Barnett JH., *et al.* "Cognitive reserve in neuropsychiatry". *Psychological Medicine* 36.8 (2006): 1053-1064.
26. Marcantonio ER., *et al.* "Reducing delirium after hip fracture: A randomized trial". *Journal of the American Geriatrics Society* 49.5 (2001): 516-522.
27. Naughton BJ., *et al.* "A Multifactorial Intervention to Reduce Prevalence of Delirium and Shorten Hospital Length of Stay". *Journal of the American Geriatrics Society* 53.1 (2005): 18-23.
28. Bender R and Lange S. "Adjusting for multiple testing - when and how?" *Journal of Clinical Epidemiology* 54.4 (2001): 343-349.
29. Zimmerman RA and Bilaniuk LT. "Age-related incidence of pineal calcification detected by computed tomography". *Radiology* 142.3 (1982): 659-662.
30. Dandy WE and Blackfan KD. "Internal hydrocephalus: an experimental, clinical, and pathological study". *American Journal of Diseases Of Children* 8 (1914): 406-482.
31. Groswasser Z., *et al.* "Incidence, CT findings and rehabilitation outcome of patients with communicative hydrocephalus following severe head injury". *Brain Injury* 2.4 (1988): 267-272.
32. Mazzini L., *et al.* "Posttraumatic hydrocephalus: a clinical, neuroradiologic, and neuropsychologic assessment of long-term outcome". *Archives of Physical Medicine and Rehabilitation* 84.11 (2003): 1637-1641.
33. Bontke CF. "Medical complications related to traumatic brain injury". *Physical Medicine and Rehabilitation* 3 (1989): 43-58.
34. Narayan RJ., *et al.* "Neurologic sequelae of head injury". Rosenthal M, ed. *Rehabilitation of the Adult and Child With Traumatic Brain Injury*. 2nd edition Philadelphia, Pa: Davis (1990): 94-106.
35. Stein S and Schrader P. "Neurologic sequelae". *Physical Medicine and Rehabilitation* 4 (1990): 543-557.

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