



SYSTEMATIC REVIEWS (WITH OR WITHOUT META-ANALYSES)

Head computed tomography findings in geriatric emergency department patients with delirium, altered mental status, and confusion: A systematic review

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Abstract

Background: Delirium, altered mental status (AMS), or confusion among older adults are common presentations to the emergency department (ED). We aimed to report the proportion of older ED patients presenting with delirium who have acute abnormal findings on head imaging. We also assessed whether anticoagulation, neurological deficits, trauma, or headache were associated with head imaging abnormalities in these patients.

Methods: A systematic review was performed using Ovid Medline, Embase, Clinicaltrials.gov, Web of Science, and Cochrane Central from conception to April 8, 2021. Citations were included if they described patients aged 65 years or older who received neuroimaging at the time of ED assessment for delirium, confusion, or AMS. Screening, data extraction, and bias assessment were performed in duplicate. The estimated proportion of patients with abnormal neuroimaging and odds ratios (ORs) for each predictor were calculated.

Results: The search strategy identified 3014 unique citations, of which six studies reporting on 909 patients with confusion or AMS were included. None of the studies formally diagnosed delirium. Overall, the proportions of older ED patients with AMS or confusion were found to have an abnormal head computed tomography (CT) was 15.6% (95% confidence interval [CI] 7.3%–26.2%). The prevalence of focal neurologic findings was 13.0% (66/506) and for anticoagulation was 9.8% (33/337) among the studies who reported them. The presence of a focal neurological deficit was associated with abnormal head CT (OR 101.8, 95% CI 30.5–340.1). Anticoagulation was not associated with abnormal head CT (OR 1.2, 95% CI 0.4–3.3). No studies reported on the association between headache or trauma and abnormal neuroimaging.

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Conclusions: The proportion of abnormal findings on CT neuroimaging in older ED patients with AMS or confusion was 15.6%. The presence of a focal neurological deficit was a strong predictor for the presence of acute abnormality, whereas anticoagulation was not.

INTRODUCTION

Background

Delirium is a common and serious brain dysfunction affecting older adults, causing symptoms of confusion, altered level of consciousness, inattention, and perceptual disturbances.¹ Altered mental status (AMS) among older adults is a common presentation to the emergency department (ED), and many of these patients meet the criteria for delirium. It is estimated that 6%–38% of older ED patients have delirium.^{2–4} Delirium is associated with higher death rates and accelerated functional decline. On a system level, delirium costs are estimated to be up to \$152 billion each year.^{1,5} Delirium screening, treatment, and prevention has been the focus of many geriatric initiatives, including the current multidisciplinary geriatric ED guidelines.⁶

Rationale

Delirium etiologies are diverse and multifactorial including infection, medications, pain, surgery, acute medical illness, drug intoxication, immobilization, metabolic derangement, sleep deprivation, and acute neurological disease.^{7–13} Neurological etiologies for delirium include intracranial hemorrhage, ischemic stroke, and brain tumor, all of which are diagnosed with computed tomography (CT) imaging or magnetic resonance imaging (MRI).^{3,14} Head CT is commonly used as part of the evaluation of neurologic emergencies in the ED, and overutilization has been reported.^{15,16} Considerable variability in ED CT scan ordering exists for older adults with neurologic findings.¹⁷ There is no consensus regarding who requires a head CT when diagnosed with delirium.^{18,19}

Objective

We undertook a systematic review and meta-analysis to evaluate CT scan results in older ED patients with delirium. Our primary goal was to determine the rate of acutely abnormal head CT among older adults who received a CT during the ED evaluation for delirium, confusion, or AMS. Furthermore, we aimed to synthesize the literature on the association between four risk factors: headache, focal neurological deficit, trauma, and anticoagulation use, with abnormal ED head CT imaging among older adults with delirium. Our PICO question was as follows:

- Population: Patients 65 and older, with delirium who had head imaging;

- Intervention/Exposure: Abnormal neurologic exam, headache, trauma, anticoagulation;
- Control: Normal exam, not on anticoagulation, no headache, no trauma;
- Outcome: Acute abnormality on head imaging (MRI/CT) as the possible/likely etiology of delirium.

METHODS

Overview

This article was written in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.²⁰

Search strategy and study eligibility

We searched the published literature using search strategies created by a medical librarian for CT or MRI brain scans in older patients presenting to the emergency department with delirium (Appendix A). The search strategies were established using a combination of standardized terms and key words, including but not limited to (delirium OR confusion OR acute mental status change) and (computed tomography OR MRI) AND (emergency department OR acute care OR emergency physician). The search was run on April 8, 2021, using an age exclusion filter to restrict to adults in the databases Ovid Medline 1946–, Embase.com 1947–, Web of Science 1900–, Cochrane Central, Pubmed Central, and Clinicaltrials.gov. A total of 3493 citations were exported to Endnote. A total of 479 duplicates were assumed to be accurately identified and removed for a total of 3014 unique citations. These citations were stored in Covidence systematic review software, Veritas Health Innovation, Melbourne, Australia.

We included original studies reporting on patients aged 65 years of age or older who received CT or MRI neuroimaging at the time of assessment in the ED for delirium, confusion, or AMS. We accepted papers with a study population defined by the terms AMS/confusion, as there is a significant overlap between these terms and delirium. We also included patients with delirium superimposed on dementia. We defined ischemic stroke, hemorrhage, and brain mass as acute findings on head CT. Studies were included if 80% or more of the total study population met our inclusion criteria or the authors provided data for the subset of patients that met our inclusion criteria. We included both published articles and conference abstracts.

We excluded citations reporting on hospitalized inpatients, patients with chronic confusion who are presenting at their baseline, and studies reporting only on subgroups of delirious patients (such as focusing solely on trauma patients or patients with cancer). Case reports were also excluded. The title and abstract of each reference were independently screened by two team members based on the inclusion and exclusion criteria, with a third team member acting as the tiebreaker when needed. All team members then engaged in full-text review so that each study was independently reviewed by two team members for final inclusion in this systematic review, with a third team member again acting as the tiebreaker when needed.

Data extraction and quality assessment

Three team members independently extracted data from the studies with disagreements resolved by discussion. The data were extracted using a template created by the investigators that included the following: (a) study author, years of conduct, research design, and sample size; (b) population characteristics (age, sex); and (c) abnormal head CT findings (number and diagnosis). When available, we also extracted the presence and absence of anticoagulation use, trauma, headache, and focal neurological deficit. Authors of several studies were contacted to obtain primary data when the results were reported in a manner that would not allow accurate or complete data extraction from their article for the purposes of our meta-analysis.

Two team members independently assessed the risk of bias of each study using the Tool to Assess Risk of Bias in Longitudinal Symptom Research Studies Aimed at the General Population from the Clarity Group at McMaster University, with a third team member acting as the tiebreaker when needed.²¹ The tool covers the following domains: representativeness of the general population, accuracy of the assessment of the outcome, and completeness of the data, categorizing studies as having a low, intermediate, or high risk of bias.

Statistical analysis

Meta-analysis was performed to calculate the pooled random effects estimated proportion and 95% confidence interval (CI) of patients with abnormal neuroimaging. Odds ratios (ORs) with 95% CIs were calculated for each predictor. Heterogeneity was assessed using I^2 . MedCalc statistical software v20.019 (MedCalc Software Ltd) was used for meta-analysis calculations.

RESULTS

Study characteristics

The search strategy identified a total of 3014 studies. There were 2967 studies that were excluded during the title and abstract screen for either not meeting our inclusion criteria or being a duplicate.

Forty-seven studies underwent full-text review, resulting in six studies being deemed appropriate for inclusion in this systematic review. Details of the selection process can be found in [Figure 1](#).

The six studies that were identified all examined CT imaging; none focused on MRI imaging.^{18,22-26} With the exception of one study,¹⁸ all were retrospective cohort studies and they were conducted in a single ED. The total sample included 909 patients. All papers focused on patients with either an acute change in mental status or confusion. None of the papers specifically diagnosed patients with delirium by applying its diagnostic criteria.

Five studies focused only on older adults aged 65 or above. One study included adult patients; we reported the data on the subset of patients aged 65 or above.²⁵ Reported abnormal CT findings were described as either "acute" or "clinically significant," with four of the six studies explicitly defining these terms.^{18,24-26} Detailed characteristics of each of the studies are presented in [Tables 1](#) and [2](#). The proportion of acute abnormal head CTs by study is shown in [Table 3](#). Of note, the study by Choi et al.²² included older adults with fever. This cohort may not be generalizable to all older ED patients with AMS or confusion. We performed a sensitivity analysis without the study by Choi et al., which is reported below.

Synthesis of results

[Table 3](#) demonstrates the pooled as well as each study's proportion of abnormal head CT. The pooled proportion was 15.6% (95% CI 7.3%-26.2%) and I^2 was 94.6% indicating substantial heterogeneity with a $p < 0.0001$. [Figure 2](#) demonstrates the corresponding forest plot.

Risk factors for abnormal head CT

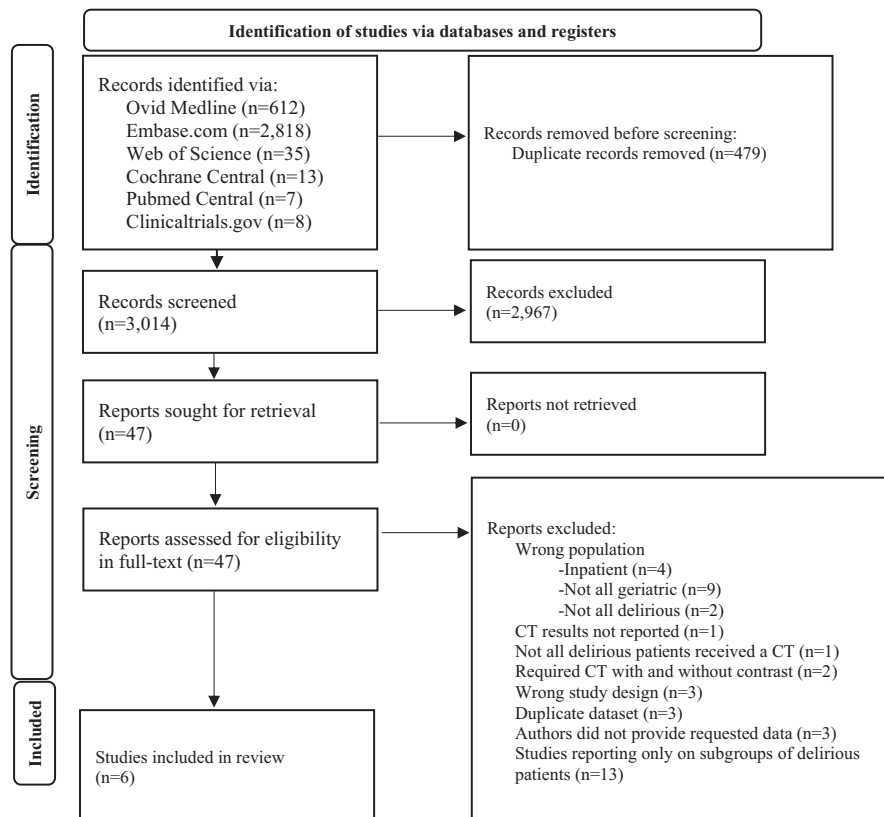
Anticoagulation

Two studies (Choi et al.²² and Lloyd et al.²⁴) examined anticoagulation as a risk factor for an abnormal head CT. The prevalence of anticoagulation in the two studies was 33/366 (0.08). [Table 4](#) lists the pooled OR for abnormal head CT findings among patients taking anticoagulant medications (1.18, 95% CI 0.43-3.25), with I^2 of 0, indicating no association between anticoagulation and acutely abnormal head CT. [Figure 3](#) demonstrates the associated forest plot. Das et al.²³ reported that 15/99 (15.1%) of patients scanned were on anticoagulation. However, they could not find documentation of whether patients were on anticoagulation among 12 patients. Hence, we excluded the study from meta-analysis of anticoagulation as a risk factor.²⁴

Focal neurological deficits

We also examined whether the finding of a focal neurologic deficit predicted acutely abnormal head CTs. Two studies (Choi et al.²² and

FIGURE 1 Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flowchart



Shin et al.²⁶ were included. Hardy and Brennan¹⁸ reported acute neurologic signs in their study, but not all patients had a neurologic exam, even among those with abnormal head CTs. Hence, we excluded the study from meta-analysis of the focal neurologic deficits. The prevalence of focal neurological deficit in the two studies was 0.13 (55/506). The prevalence of focal neurological deficit in the two studies was 0.13 (55/506). In pooled meta-analysis, the OR of an acutely abnormal head CT among patients with a focal neurologic deficit was 110.2 (95% CI 30.5–340.1); I^2 was 0 (Table 5). Figure 4 illustrates the associated forest plot.

Trauma

Three of the studies included in our review excluded patients with trauma,^{22,24,26} and only one study examined trauma as a risk factor for an acutely abnormal head CT.²⁵ Hardy and Brennan¹⁸ reported that 22 patients fell overall (22/106, 20.7%), but did not report how many falls were among the number of patients with abnormal CTs. This limits our ability to report any association.

Headache

No studies reported on the association between history of headache and abnormal neuroimaging among patients with confusion or AMS among older patients.

Risk of bias

Only one study was rated as having low risk of bias across all categories, two studies had low or intermediate risk, and three studies had intermediate or high risk of bias across domains. Risk of bias results are shown in Figure 5.

Sensitivity analysis

Our Appendix Table reports our sensitivity analysis, which excluded the study by Choi et al. given that it focused on patients with fever. The pooled proportion of abnormal head CTs did not change significantly at 15.3 (95% CI 5.1–29.8).

DISCUSSION

We found that 16% of head CTs ordered in the ED on older adults presenting with delirium, AMS, or confusion had an acutely abnormal finding. Anticoagulation was not associated with an abnormal head CT and findings of a focal neurologic deficits greatly increased the odds of an abnormal head CT. We were unable to comment on the association of headache or trauma with an abnormal head CT. Since we defined an abnormal finding of ischemia, hemorrhage, and mass, the proportion of abnormal CTs implies that brain imaging can help to identify an etiology for delirium, confusion, or AMS. The probability of finding

TABLE 1 Characteristics of included studies

First author, last name	Publication year	Study design	Condition	Study period	Country	Age (mean \pm SD or median [IQR]) or age range	Proportion of male participants	Inclusion/exclusion
Choi ²²	2020	Retro-spective	Altered mental status	Jul 2016–Jun 2019	Korea	≥ 65 78 \pm 7.2	48%	Included: febrile patients Excluded: patients without brain imaging, history of trauma
Das ²³	2013	Retrospective	Altered mental status	Jan 2009–Dec 2011	USA	≥ 65 Mean not reported	Not reported	Included: patients ≥ 65 with AMS
Hardy ¹⁸	2008	Prospective	Confusion	May 2007–Jul 2007	Australia	71–97, Mean age 83, SD not reported	Not reported	Included: patients > 70 with new-onset confusion and had noncontrast head CT, Excluded: patients with no change to longstanding confusion
Lloyd ²⁴	2019	Retrospective	Confusion	Not reported	UK	85 and above, mean/median not reported	Not reported	Included: patients > 85 with new confusion Excluded: lateral neurologic signs or clearly witnessed trauma/head injury
Nesselroth ^{25a}	2021	Retrospective	Confusion	Jan 2017–Feb 2017	Israel	≥ 65 , mean/median not reported	Not reported	Included: patients with noncontrast head CT scans Excluded: patients < 18 and incomplete radiology reports
Shin ²⁶	2018	Retrospective	GCS < 15, acute AMS	Apr 2014–Dec 2014	Korea	≥ 65 , mean \pm SD 77 \pm 7.0	46%	Included: patients without trauma, those with GCS ≤ 14 , those with noncommunicable disease. Excluded: patients with previous neurologic deficit, alcohol, cardiac arrest, < 18, recovered from mental illness

Abbreviations: AMS, altered mental status; GCS, Glasgow Coma Scale; IQR, interquartile range.
^aSubset patient population.

TABLE 2 Rate of abnormal head CT scans among older patients with AMS or confusion

First author, last name	Publication year	N	Risk factors: AC, FD, Trauma, Headache	Acute abnormal head CT, n (%)	Abnormal head CT abnormality, if reported, some had two abnormalities
Choi ²²	2020	285	AC = P FD = P Trauma = NR Headache = NR	47 (16.5%)	19 Ischemic strokes 20 ICH 6 Brain mass 3 Other
Das ²³	2013	100	AC = NR FD = NR Trauma = NR Headache = NR	2 (2.0%), Rate = 2.0	Not reported
Hardy ¹⁸	2008	106	AC = NR FD = P Trauma = P Headache = NR	15 (14.1%)	10 Ischemic stroke 4 ICH 2 Brain mass
Lloyd ²⁴	2019	111	AC = P FD = NR Trauma = NR Headache = NR	12 (10.8%)	4 Ischemic stroke 7 ICH 1 Other
Nesselroth ^{25,a}	2021	86	AC = NR FD = NR Trauma = NR Headache = NR	17 (19.8%)	Not reported
Shin ²⁶	2018	221	AC = NR FD = P Trauma = NR Headache = NR	81 (36.7%)	42 Ischemic stroke 33 ICH 6 Brain mass

Abbreviations: A, absent; AC, anticoagulation; AMS, altered mental status; FD, focal deficits; GCS, Glasgow Coma Scale; ICH, intracranial hemorrhage; IQR, interquartile range; NR, not reported; P, present.

^aSubset patient population.

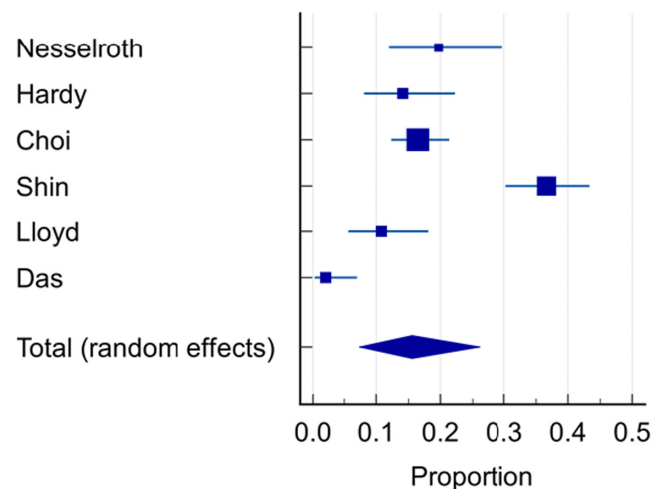
TABLE 3 Proportion of acute abnormal head CT among patients with delirium, AMS, or confusion, based on pooled data

Study	Sample size	Proportion (%)	95% CI
Nesselroth ²⁵	86	19.8	12.0–29.8
Hardy ¹⁸	106	14.2	8.1–22.3
Choi ²²	285	16.5	12.4–21.3
Shin ²⁶	221	36.7	30.3–43.4
Lloyd ²⁴	111	10.8	5.7–18.1
Das ²³	100	2.0	0.2–7.0
Total (random effects)	909	15.6	7.3–26.2

Abbreviation: AMS, altered mental status.

an abnormal head CT will likely increase if there is a report of falls and trauma, though this could not be confirmed from our review.

Previous geriatric ED guidelines have not addressed the evaluation of delirium due to a lack of data.²⁷ In the inpatient setting, studies have reported that head CTs are of low diagnostic yield for delirium and AMS.^{28,29} One retrospective study of medical ICU patients found the most common indication for a head CT was AMS,²⁸ yet the authors determined that it has a low diagnostic value and is likely overused.²⁸ Another study also reported a low diagnostic yield of head CTs among delirious patients admitted to general medicine

**FIGURE 2** Forest plot of delirium, AMS, and confusion and acutely abnormal head CT. AMS, altered mental status

or medical subspecialty units.²⁹ The authors conclude that the routine use of head CT in evaluation delirium in hospitalized patients is unnecessary.²⁹ However, these studies may have limited generalizability to the ED. Two recent narrative reviews published by our group on the evaluation of delirium reveal a paucity of evidence regarding the clinical utility of head CT in older adults with delirium

Study	Exposure	Controls	OR	95% CI	z	p	Weight (%)
							Random
Choi ²²	4/18	43/267	1.5	0.5–4.7			77.2
Lloyd ²⁴	1/15	10/84	0.5	0.1–4.5			22.8
Total (random effects)	5/33	53/351	1.2	0.4–3.3	0.3	0.8	100.0

TABLE 4 Meta-analysis of OR of anticoagulation and association with acutely abnormal head CT

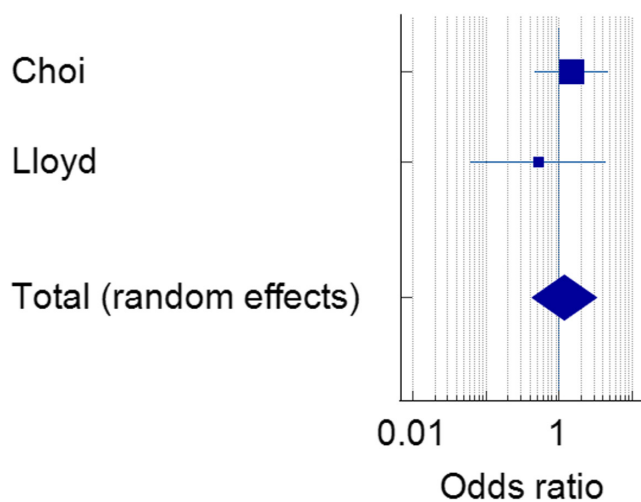


FIGURE 3 Forest plot of patients with delirium, AMS, and confusion on anticoagulation and acutely abnormal head CT. AMS, altered mental status

in the ED.^{30,31} In contrast, the main findings from this systematic review are the rate of abnormal head CTs among those ordered in older adults with delirium in the ED, the association between focal neurological deficits and abnormal head CTs, and the lack of association between anticoagulation and head CTs.

Our findings are consistent with other rates of abnormal head CTs found in the literature. Wang and You³² conducted a review of CT scans of nontrauma ED patients and found that 13.8% (548) of patients had head CTs with clinically important abnormalities. Of the patients with an AMS, they found an adjusted OR of 2.32 for abnormal head CTs. However, our study only included older patients and those confused, whereas Wang and You³² included all patients 18 and older and did not report the specific rate of abnormal head CTs among AMS patients. Similarly, Covino et al.³³ found the rate of abnormal head CTs to be 15.2% among a predefined cohort of adult patients with neurological deficits, postural instability, acute headache, AMS, seizures, confusion, dizziness, vertigo, syncope, and presyncope. They found an OR of 2.8 (95% CI 2.0–4.0) among those with altered state of consciousness and an OR of 5.4 (95% CI 3.7–7.8) among those with confusion.³³ However, similar to Wang and You,³² the study by Covino et al.³³ did not limit their study to older patients or those only with delirium.

Our study did not show that anticoagulation predicted acutely abnormal head CTs. Although Wang and You³² found that derangements in coagulation predicted abnormal head CT with adjusted OR

1.91, Covino et al.³³ also did not find that oral anticoagulant therapy predicted abnormal head CTs with an OR of 1.7 (95% CI 0.9–3.1). The incidence of intracranial hemorrhage reported in similar studies of the nonanticoagulated population is between 4% and 7%.^{34,35} However, our systematic review only included two studies and 33 patients on anticoagulation so conclusions are limited.

We found that focal neurologic deficits strongly predicted an abnormal head CT (OR 110.2, 95% CI 30.5–340.1). Our findings are similar to other studies. The study by Wang and You³² also found that focal neurologic deficit predicted abnormal head CT adjusted OR 5.39 (95% CI 3.90–7.47). Covino et al.³³ found that any neurological deficit found on physical examination had an OR of 11.1 (95% CI 7.4–16.6) for abnormal head CT. In a retrospective review of 500 nontrauma adult ED patients by Bent et al.,³⁶ abnormal CTs were found in 51 of 500 patients (10.1%). Only age > 55 and focal neurologic deficit (adjusted OR 20.7, 95% CI 9.4–45.7) were associated with positive head CTs. Hence, any geriatric patients with delirium, confusion, or AMS with a new focal neurologic deficit should undergo head imaging, such as a head CT. Although we did not have studies that addressed trauma among delirious patients, most likely those who sustained trauma and presenting to ED with AMS will need to get brain imaging.

LIMITATIONS

There are several limitations to this systematic review and meta-analysis. First, our study focused on older adults with confusion or AMS, rather than those with a formal diagnosis of delirium, due to lack of literature focusing only on patients with delirium. However, older adults with a chief complaint of AMS are highly likely to be delirious, validating our current approach.¹ AMS is only about 40% sensitive for delirium, so there are likely patients with delirium who are missed from these studies.¹ Second, our reported proportion of abnormal head CTs is among older adults with delirium those who received a head CT in the ED, rather than all patients with delirium. Combined with the estimated frequency of missed delirium, which can be up to 80%,³⁷ the true proportion of acute head CT abnormalities in patients with delirium is likely much lower. Third, measurement bias can be present as two of the studies did not explicitly define “abnormal head CT,” although they were described as “acute” or “clinically significant.”^{22,23} We deferred to the original studies’ definition of terms such as acute findings or focal neurologic deficits which may affect the calculated prevalence of risk factors. We did

TABLE 5 Meta-analysis of focal neurologic deficits among patients with confusion, delirium, or AMS, and acutely abnormal head CT

Study	Exposure	Controls	OR	95% CI	p	Weight (%)
Choi ²²	8/9	39/276	48.6	5.9–399.5		32.8
Shin ²⁶	55/57	26/164	146.0	33.5–636.0		67.2
Total (random effects)	63/66	65/440	101.8	30.5–340.1	<0.001	100.0

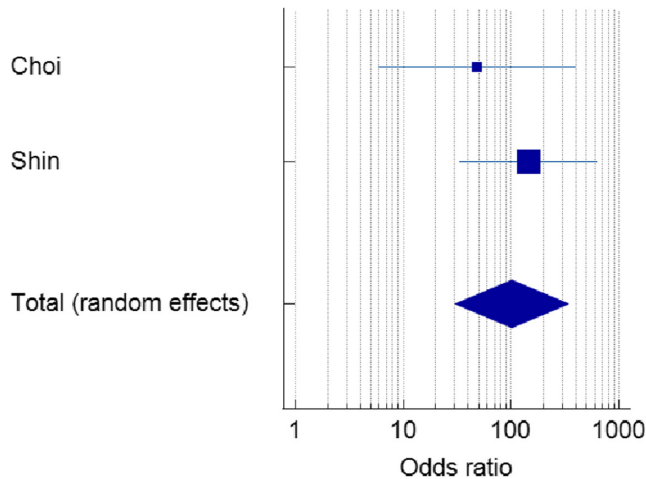


FIGURE 4 Forest plot of patients with delirium, AMS, and confusion with acute focal neurologic deficits and acutely abnormal head CT. AMS, altered mental status

use a consensus definition of acute findings that included ischemic stroke, hemorrhage, and brain mass in our review. However, a consistent definition of focal neurological deficits was difficult to identify from included studies. Fourth, we found only a small number of mostly retrospective, generally low-quality studies, reporting associations between our baseline predictors of interest and abnormal head imaging. Given our inclusion criteria included patients over 65 who had imaging in the ED and were confused, our study may have missed studies that may have examined headache and trauma as risk factors but been excluded because patients were not older or confused.

CONCLUSIONS

We conclude that around 16% of older ED patients with delirium who received a head computed tomography have an acutely abnormal head computed tomography and that the presence of neurological deficit is a strong indicator for abnormal head computed tomography. This included brain pathology, which required both surgical intervention and medical management. The recommendation for brain imaging for all delirious older adults in the ED will require a further step in a careful assessment of the existing evidence, benefits, and drawbacks using the GRADE approach.³⁸ As the geriatric ED guidelines are utilizing the GRADE approach for their

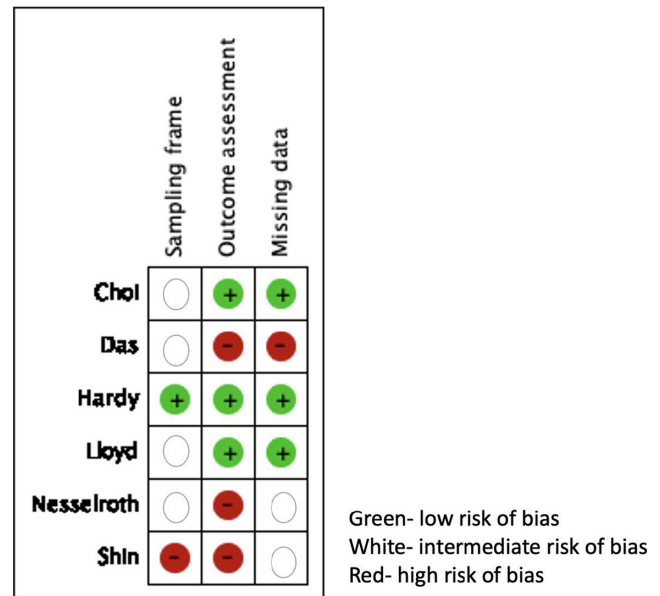


FIGURE 5 Risk-of-bias figure for selected studies

recommendations, our recommendations as to whether head imaging should be done on patients with delirium, confusion, or altered mental status will follow the GRADE methodology and be combined with recommendations on two other delirium population, intervention, control, outcome questions in a subsequent article. These findings will potentially inform our recommendations in the upcoming geriatric ED guidelines but our studies show there are many gaps in the literature. Future studies should include head imaging as it relates to formal diagnoses of delirium and delirium subtypes as well as more prospective studies with clear definitions of risk factors.

AUTHOR CONTRIBUTIONS

Shan W. Liu, Sangil Lee, Danya Khoujah, Alexander X. Lo, Kerstin de Wit, and the Geriatric Emergency Department Delirium Guidelines authors all conceived of the question and study design. Michelle Doering conducted the search of the literature. Shan W. Liu, Sangil Lee, Jane M. Hayes, Danya Khoujah, Alexander X. Lo, Kerstin de Wit conducted abstract review and selection of full text. Shan W. Liu, Sangil Lee conducted data analysis. Sangil Lee, Michelle Doering, Jane M. Hayes and Shan W. Liu drafted the manuscript. All authors contributed substantially to its revision. Shan W. Liu and Sangil Lee take responsibility for the manuscript as a whole.

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CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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