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Delirium in the emergency department: science or ritual? Rethinking diagnostic pathways in emergency delirium management

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Abstract

Delirium is an acute disturbance of attention and awareness that develops over a short period and typically fluctuates in severity. It may affect up to one-quarter of older adults presenting to the Emergency Department (ED) and is associated with increased mortality, prolonged hospital stays, and increased healthcare costs. Despite its clinical importance, delirium is frequently underrecognized, as it may manifest with subtle or nonspecific symptoms. When delirium is suspected, prompt and systematic evaluation is critical for identifying underlying etiologies, which may include infections, metabolic disturbances, structural brain pathology, or adverse drug effects. This article is hence aimed to provide a critical overview of the English-language literature published between the years 2020 and 2025 on laboratory investigations and diagnostic workup of delirium in older patients presenting to the ED.

Introduction

Delirium, the most frequent complication in older hospitalized patients, is an acute neuropsychiatric syndrome defined by disturbances in attention, awareness, and cognition, typically with a fluctuating course. Epidemiological evidence indicates that it affects approximately one in four older adults in general medical settings and Emergency Departments (EDs). Delirium should not be regarded as a benign condition, as it is strongly associated with adverse outcomes such as prolonged hospital stay, falls, immobilization, functional decline, new institutionalization, long-term cognitive impairment, and up to a 2-fold increase in short-term mortality.[1,2]

The diagnosis of this condition has recently improved due to the widespread use of structured screening tools. The 4AT has become the most widely adopted approach, thanks to its brevity, sensitivity, and applicability in emergency and acute care settings.[3] Nevertheless, screening is only the first step. Once delirium is identified, the diagnostic journey must pivot from protocol-driven checklists toward specific clinical reasoning and evaluation. The workup should begin with taking a comprehensive medical history, including collateral information, and an accurate physical examination to identify reversible precipitants, such as infections, metabolic disturbances, sensory deprivation, adverse medication effects, urinary retention, constipation, or environmental stressors. In fact, the origin of delirium is usually multifactorial, resulting from an interplay between predisposing factors (e.g., age, dementia, sensory impairment, frailty, polypharmacy) and precipitating factors (e.g., acute illness, surgery, dehydration, medications).[4] Without a structured clinical approach, diagnostic testing can become indiscriminate, expensive, and misleading. The goal is not only to confirm delirium, but also to determine the underlying causes and address those factors.

Clinical scenario

An 81-year-old woman was admitted to the local ED for acute confusion and disorganized speech. According to her son, she experienced alterations in mental status for several days. Her past medical history was notable for type 2 diabetes mellitus, hypertension, and mild dementia. She had no fever, reported no pain, and exhibited no

other acute symptoms. Upon examination, she appeared calm and was seated quietly in bed; however, she was inattentive and did not respond appropriately to questions. The attending physician initiated the so-called “full delirium panel”, *i.e.*, a broad diagnostic workup including a non-contrast head CT, complete blood tests, urinalysis, electrocardiogram, chest radiograph, and abdominal ultrasonography. After approximately 5 hours, the patient became increasingly agitated and began pacing back and forth in the ED. This clinical course raises the critical question: “could we have done (more or) better?”

Materials and Methods

The objective of this review was to identify and summarize recent evidence specifically addressing the diagnostic workup of delirium in older adults presenting to the ED. To achieve this goal, we conducted a narrative literature search focusing on studies published within the past five years. In July 2025, we systematically searched PubMed and Google Scholar using combinations of the following keywords: “workup,” “laboratory,” “delirium,” “older patient,” and “emergency department.” The search was restricted to English-language documents published between January 2020 and July 2025.

Eligible sources included full-text original research articles, narrative and systematic reviews, and clinical practice guidelines that described diagnostic pathways or laboratory/imaging investigations for identifying underlying or reversible causes of delirium in the ED setting. Titles and abstracts were screened for relevance, and full texts of potentially eligible studies were reviewed. Key data were extracted, and findings were integrated narratively, with emphasis on identifying commonalities, gaps, and areas of divergence across published diagnostic recommendations. Our exclusion criteria included editorials or conference abstracts not focused on delirium screening in EDs, as well as those that did not meet the above-mentioned inclusion criteria (Figure 1).

Results

General approach

Our search yielded a total number of 21 documents. After screening titles and abstracts, 7 records were excluded as they were not pertinent to the aims of this review. Following full-text assessment, 14 publications met the eligibility criteria and were included in the final narrative synthesis (Table 1). All reviewed sources consistently emphasized that a careful history and thorough physical examination should fundamentally drive the diagnostic evaluation of delirium. Lee and colleagues[5] emphasized that, once delirium is suspected, emergency physicians should obtain a comprehensive clinical history, actively search for potential precipitating factors, and use these findings to guide the selection of laboratory and radiographic investigations, rather than pursuing indiscriminate testing. Goldhar and Frank's "DIMS-PLUS5" framework[6] provides a structured taxonomy of common delirium precipitants, including Drug effects, Infection, Metabolic disturbances, and Structural/systemic causes, while also incorporating additional domains such as Pain, Liquids & solids (nutrition and hydration), Urine & bowels, Senses, Sleep, Setting, Stasis, and Stress. This systematic checklist encourages clinicians to consider both medical and environmental contributors, thus improving diagnostic accuracy and comprehensiveness. Similarly, Marcantonio[7] proposed the mnemonic DELIRIUM, which integrates the most frequently encountered reversible causes into a practical bedside tool, reinforcing the central role of structured frameworks in guiding efficient and targeted diagnostic workups: Drugs; Electrolytes disturbances/Eyes/Ears; Low oxygen/Lack of analgesia; Infections; Retention (urinary/stool), Restraints; Ischemia, Intracranial disorders; Underhydration, Undernutrition; Metabolic disorders/Myocardial disorders.

Routine laboratory and diagnostic tests

Laboratory and diagnostic testing play a crucial role in evaluating delirium, but their appropriateness depends on careful clinical reasoning rather than a stepwise or protocol-driven approach. In the ED, the choice of diagnostic tests should be guided primarily by specific clinical suspicion arising from history, collateral information, physical examination, and assessment of vital signs. Basic investigations, such as complete blood count, metabolic panel, bedside blood glucose measurement, urinalysis, electrocardiogram, and chest radiography, are commonly performed when clinically indicated. More advanced or second-line investigations, including brain imaging (CT or

MRI), lumbar puncture, electroencephalography, extended microbiological cultures, endocrine testing, or other targeted examinations, are not routinely available in most EDs and should be reserved for selected patients with well-defined clinical indications. When these investigations are required, patients usually need to be admitted to an emergency observation unit or to an inpatient hospital ward, where further diagnostic evaluation can be safely and more appropriately completed.

Several sources caution against indiscriminate testing instead. The important review by Echeverría *et al*.[9] emphasizes the importance of prioritizing investigations based on the most likely clinical suspicions, warning that extensive or unnecessary procedures may increase patient distress and exacerbate agitation. Similarly, the Cambridge guideline[1] highlights that diagnostic choices should be context-specific and tailored to local resource availability. When no cause is apparent after standard evaluation, clinicians should consider less common but clinically important etiologies such as seizures, carbon monoxide poisoning, encephalitis, Wernicke encephalopathy, adrenal crisis, or sepsis from occult sources.[9]

Recent research has moved beyond traditional classifications of delirium, which were largely based on psychomotor subtype (hyperactive, hypoactive, mixed) or risk factors, toward etiologically driven and data-derived subtyping. Cirbus *et al.*[10] proposed clinically meaningful etiologic categories, including hypoxic, septic, metabolic, medication-related, and multifactorial delirium, each associated with distinct prognostic trajectories and therapeutic implications. In parallel, Potter *et al.*[15] applied unsupervised machine learning to intensive care cohorts and derived four distinct subtypes characterized by differing patterns of organ dysfunction, inflammatory response, sedative exposure, and clinical outcomes. These findings suggest that diagnostic strategies should increasingly be tailored to general clinical algorithms, but also to suspected delirium subtypes. For example, hypoactive delirium with suspected metabolic basis may warrant early targeted metabolic and nutritional assessment, whereas hyperactive presentations with potential drug-related triggers may prompt toxicology screening and sedative load evaluation.

Importantly, all diagnostic evaluations must be undertaken alongside the immediate implementation of non-pharmacological management strategies, such as reorientation, hydration, mobilization, the use of sensory aids, and the promotion of sleep hygiene,

while simultaneously addressing the underlying cause.[11] This integrated approach balances timely identification of reversible factors with supportive care, thereby optimizing outcomes in this vulnerable patient population.

Summary of recommended investigations

A systematic approach based on a structured yet personalized diagnostic evaluation, which prioritizes the most likely etiologies, is the most effective way to minimize unnecessary testing and patient burden (Figure 2).

The initial assessment should include measurement of vital signs, namely pulse oximetry, blood pressure, heart rate, respiratory rate, and body temperature. When abnormalities are detected or sepsis is suspected, arterial or venous blood gas analysis, along with measurement of blood lactate, is recommended. Bedside blood glucose measurement should be performed in a timely manner to identify metabolic contributors, namely hypo- or hyperglycemia. Evaluation for suspected infection should include complete blood count, urinalysis, and chest radiography. Although blood and urine cultures are always indicated when an infection is suspected, clinicians must interpret positive results cautiously, as asymptomatic bacteriuria is relatively common in older adults.[1,8,9] Basic or comprehensive metabolic panels in patients with suspected electrolyte imbalance or renal dysfunction should assess urea, creatinine, sodium, potassium, calcium, magnesium, and phosphate.[6] In patients with suspected hepatic failure or metabolic encephalopathy, liver function tests and serum ammonia should be ordered.[1,5] Thyroid function tests (namely Thyroid-Stimulating Hormone, TSH) are recommended as routine diagnostics; cortisol or other adrenal function tests should be considered only when clinically indicated.[6,8] Electrocardiography is advisable for all patients, with cardiac troponin assessment when ischemia is suspected.[5] Medication review and targeted drug level testing (e.g., digoxin, lithium, acetaminophen, salicylate, ethanol) should be performed, with urine toxicology added when overuse/intoxication is suspected.[1,6] Non-contrast CT or magnetic resonance imaging of the head should be performed in cases of recent head trauma, new focal neurological deficits, or unexplained persistent delirium.[6,9] Electroencephalography (EEG) is indicated for assessing nonconvulsive status epilepticus, and lumbar puncture should be performed when meningitis or encephalitis are suspected.[5,8] Additional

investigations, such as abdominal imaging, vitamin B_{12} and thiamine levels, and other targeted tests, should be guided by clinical judgment and specific risk factors.[6,9]

Discussion

Delirium may represent a true medical emergency, so that a prompt and systematic evaluation for underlying acute diseases and other conditions that disrupt orientation in space and time should be performed when suspected. The primary objective of diagnostic testing is to identify treatable abnormalities that may precipitate or exacerbate delirium. Early recognition and correction of these factors facilitate resolution of delirium itself. Equally important is the role of testing in ruling out alternative diagnoses that may mimic acute confusion, such as myocardial infarction, stroke, or encephalitis.

Evaluation of delirium in older patients presenting to the ED requires balancing comprehensiveness with efficiency. Current literature from 2020 to 2025 emphasizes that the diagnostic workup should be guided by a detailed history, accurate physical examination, and a structured framework of potential precipitating factors. Initial investigations typically include basic tests, such as blood glucose, complete blood count, metabolic panel, and electrocardiogram. More invasive or resource-intensive procedures, including neuroimaging, EEG, and lumbar puncture, should be reserved for cases with specific clinical indications.

In some cases, hospital admission becomes necessary. This may be indicated by haemodynamic instability, hypoxaemia, a suspected central nervous system infection, or an acute neurological event, the need for advanced diagnostic testing that is not typically available in the ED, persistent or severe agitation requiring close monitoring, an inability to ensure a safe discharge, or a lack of adequate social or caregiver support. Conversely, selected patients with rapidly reversible precipitants (e.g., dehydration, fecal impaction, urinary retention, hypoglycemia, medication-related delirium), stable vital signs, and reliable supervision may be appropriately managed in the ED or in an emergency short-stay/observation unit, with resolution of delirium following correction of the underlying cause.

Recent evidence also highlights that distinct delirium subtypes may correspond to different etiologies and laboratory profiles, underscoring the importance of tailoring

investigations to the individual clinical presentation. Cirbus *et al*.[10] reported that infections are frequent precipitants, with the most common sources being the lungs, urinary tract, gastrointestinal system, and skin. Metabolic and drug-related causes were found to be less common causes, but should not be overlooked. While laboratory and imaging studies remain critical, they are not intended to completely replace the essential elements of delirium management, encompassing a non-pharmacological, patient-centered approach.

Marcantonio[7] and Mello [13] recommend systematically assessing exacerbating factors such as pain, urinary retention, constipation, and sensory deprivation (absence of glasses or hearing aids). The DELIRIUM mnemonic provides a structured but holistic framework that integrates clinical reasoning, physical examination, and patient-centered care. Optimizing the environment, supporting orientation, promoting mobility, and involving caregivers are essential components of care and should be implemented alongside any diagnostic or therapeutic interventions.

Scenario resolution

All laboratory and diagnostic test results were non-diagnostic. However, a comprehensive physical examination allowed for the identification of pelvic discomfort. A subsequent rectal exam revealed fecal impaction, which was promptly relieved. Within a few hours, the patient gradually regained her baseline cognitive function, recognized her son, and resumed normal oral intake. She was subsequently discharged home.

Conclusions

The diagnosis and management of delirium require careful clinical reasoning, bedside assessment, and focus on both human and environmental factors. Laboratory investigations should not be considered a shortcut for diagnosing delirium in older ED patients. A detailed medical history and comprehensive physical examination remain the cornerstone of assessing delirium in short-stay units, such as the ED. Laboratory testing should be guided by the suspected delirium subtype, as emerging evidence indicates that different motor and etiologic subtypes may be associated with distinct pathophysiological mechanisms and laboratory abnormalities. This targeted approach ensures that

investigations are used to confirm or rule out specific hypotheses, rather than being indiscriminately applied.[14] Clinicians should also use structured frameworks, such as the DELIRIUM mnemonic, which emphasizes the most frequent precipitating factors (discomfort, electrolyte imbalance, local/environmental causes, infections, retention, intercurrent illness, uremia, and undesirable effects of some therapies). To the best of our knowledge, these approaches offer a practical and systematic framework for identifying reversible causes and guiding appropriate interventions.

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Figure 1 Flow Diagram Depicting Study Selection

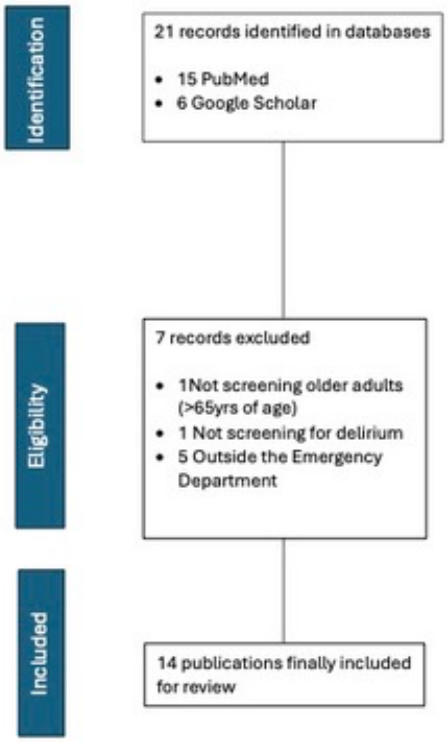

Figure 2 – Proposed investigations in patients presenting to the Emergency Department with delirium

- Pulse oximetry and arterial or venous blood gas analysis to assess hypoxemia.
- Bedside blood glucose measurement to identify hypo- or hyperglycemia.
- Complete blood count, urinalysis, chest radiography, and cultures when infection is suspected.
- Electrolytes and renal function tests to detect metabolic disturbances.
- Liver function tests and serum ammonia when hepatic or metabolic encephalopathy is suspected.
- Thyroid-stimulating hormone (TSH) and cortisol or adrenal function tests, when clinically indicated.
- Electrocardiography (ECG) and cardiac troponin when cardiac causes are suspected.
- Medication review and targeted drug level testing (e.g., digoxin, lithium, toxicology screening).
- Neuroimaging (computed tomography [CT] or magnetic resonance imaging [MRI]) in cases of trauma, focal neurological deficits, or unexplained delirium.
- Electroencephalography (EEG) and lumbar puncture when seizures or encephalitis are suspected.
- Additional investigations (e.g., vitamin B1, vitamin B12), guided by clinical judgment.

Table 1 Summary of studies included in the review.

Author (Year)	Study Type	Setting	Population	Diagnostic Framework / Focus	Key Findings / Clinical Implications
Lee et al.[5] (2021)	Narrative review	Emergency Department	Older adults	Targeted diagnostic approach	Clinical reasoning preferred over indiscriminate testing
Goldhar & Frank[6] (2022)	Narrative review	Acute care	Older adults	DIMS-PLUS5 framework	Systematic identification of multifactorial causes
Marcantonio[7] (2017)	Review	Hospital setting	Hospitalized older adults	DELIRIUM mnemonic	Structured assessment of reversible causes
Pisani[8] (2022)	Clinical guideline	ED / Acute care	Adults with delirium	BMJ Best Practice workup	Focused initial diagnostic testing
Echeverría et al.[9] (2022)	Systematic review	ED / Acute care	Older adults	Etiology-driven evaluation	Avoids over-testing and patient distress
Cirbus et al.[10] (2019)	Prospective cohort	Emergency Department	Older adults	Etiologic delirium subtypes	Different etiologies linked to outcomes

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Informed consent: not applicable.

Availability of data and materials: all data generated or analyzed during this study are included in this published article.