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REVIEW ARTICLE

Association Between Acute Kidney Injury, Delirium, and Outcomes in Patients With Critical Illness: A Systematic Review and Meta-Analysis

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OBJECTIVES: Acute kidney injury (AKI) and delirium are common complications of critical illness. However, relatively few studies have evaluated their relationship. We conducted a systematic synthesis and meta-analysis of existing evidence to clarify this association in critically ill patients.

DATA SOURCES: A comprehensive search was conducted across MEDLINE, Embase, CINAHL, Scopus, Web of Science, and Cochrane Library for publications reporting both AKI and delirium in ICUs patients from January 2000 to January 2025.

STUDY SELECTION: AKI was defined according to serum creatinine or urine output criteria based on the contemporary definitions used in the individual studies. The primary outcome was the proportion of critically ill patients with AKI who developed delirium. Secondary outcomes included mortality and health service utilization.

DATA EXTRACTION: Pooled meta-analyses were summarized as effect sizes in proportions, risk ratios (RRs), odds ratios, or weighted mean differences (WMDs) using a random-effects model. The certainty of evidence was evaluated using the Grading of Recommendations, Assessment, Development, and Evaluation approach.

DATA SYNTHESIS: Eighteen observational studies comprising 158,694 patients were included. Overall study quality was moderate. The pooled proportion of delirium among patients with AKI was 32% (95% CI, 18–47%). Delirium was associated with higher mortality (RR, 2.36; 95% CI, 1.61–3.47; moderate certainty), greater renal replacement therapy use (RR, 3.12; 95% CI, 1.89–5.15; moderate certainty), longer ICU stays (WMD, 3.54 d; 95% CI, 1.20–5.87 d; moderate certainty), and longer hospital stays (WMD, 4.78 d; 95% CI, 3.48–6.09 d; moderate certainty) compared with patients with AKI not experiencing delirium.

CONCLUSIONS: Delirium is common among critically ill patients with AKI and is associated with worse outcomes and greater health resource use.

KEYWORDS: acute kidney injury; critical care; delirium; meta-analysis; systematic review

Acute kidney injury (AKI) and acute delirium are frequent complications in critically ill patients. AKI is a highly heterogeneous condition that has consistently been associated with poorer clinical outcomes (1). Even mild or transient episodes of AKI are linked to an increased risk of both short- and long-term adverse events compared with patients without AKI. These include the development or progression of chronic kidney disease,

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KEY POINTS

Question: To date, little is known about the occurrence and outcomes of delirium among patients with acute kidney injury (AKI).

Findings: We conducted a systematic review and meta-analysis to better describe this association in critically ill patients. The pooled proportion of delirium among AKI patients was 32% and was associated with significantly higher mortality, greater renal replacement therapy use, and longer hospitalization compared with AKI patients without delirium.

Meaning: In conclusion, delirium is common in critically ill patients with AKI and is linked to worse outcomes, underscoring the need for improved recognition and monitoring strategies.

advancement to kidney failure, cerebrovascular and cardiovascular complications (2, 3), new infections and sepsis (4, 5), gastrointestinal bleeding (6), malignancy (7), bone fractures (8), and mortality (9, 10).

Delirium is another common complication of critical illness and is strongly associated with adverse outcomes such as persistent cognitive impairment, neuropsychiatric sequelae, and increased healthcare utilization (11, 12). Emerging evidence has identified distinct subphenotypes of delirium in critical illness, which may have differing prognostic implications and could inform future therapeutic strategies (13).

Experimental and clinical research has demonstrated that AKI can induce distal organ dysfunction through complex organ crosstalk, particularly affecting the heart, liver, and brain. These interactions are thought to be mediated largely by systemic and localized inflammatory cytokines, oxidative stress, and immune activation (14). In animal models of ischemic kidney injury, elevations in systemic and brain-specific inflammatory mediators have been observed, along with increased glial fibrillary acidic protein expression in astrocytes, blood-brain barrier disruption (as shown by Evans blue dye extravasation), and changes in locomotor activity after short-term injury (15). Collectively, these findings suggest that AKI may trigger both direct and indirect inflammatory and functional alterations in the brain, which could clinically present as delirium during acute critical illness (16).

Despite these insights, relatively few clinical studies have directly examined the relationship between AKI and incident delirium (17–21). Some have identified surrogate markers of AKI—such as elevated blood urea nitrogen (BUN)—as predictors of delirium within risk prediction models (22, 23). Post hoc analyses of prospective studies and clinical trials have also indicated that timely initiation of renal replacement therapy (RRT) may attenuate the link between AKI and delirium or coma (18, 24).

Current clinical practice guidelines for sedation and analgesia provide little guidance regarding the additional delirium risk among critically ill patients with AKI or its specific management (25). The true occurrence of new-onset delirium in this population remains poorly defined, as does the temporal relationship between AKI severity and delirium risk. Furthermore, the impact of RRT on the occurrence of delirium is uncertain. These represent important gaps in knowledge and clinical practice, particularly given accumulating evidence of a strong AKI-delirium association. Therefore, we conducted a systematic review and meta-analysis to evaluate the relationship between AKI and delirium in critically ill patients, aiming to consolidate existing evidence, enhance clinical understanding, and identify strategies to mitigate this complication.

MATERIALS AND METHODS

Study Design

We performed a systematic review to examine the relationship between AKI and delirium in critically ill patients. The review followed established methodological guidance from the Cochrane Collaboration and the Center for Reviews and Dissemination and was reported in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analyses statement (**Supplementary Table 1**, https://links.lww.com/CCM/H863) (26–28). Research ethics approval was not required, as the analysis incorporated only summarized data that had previously been published. The review protocol was registered in PROSPERO on March 25, 2025 (CRD420251001864).

Search Strategy

The search strategy was developed in collaboration with an experienced research librarian (J.Y.K.), who designed and implemented comprehensive searches

in Ovid MEDLINE, Ovid Embase, CINAHL, Scopus, Web of Science Core Collection, and the Cochrane Library (via Wiley). The MEDLINE search was peer-reviewed by another experienced health librarian before translating the search to other databases. To ensure comprehensive coverage, both relevant keywords and controlled vocabulary were used, incorporating the following search terms: 1) acute kidney injury, renal replacement therapy; 2) critical care, critical illness, intensive care, intensive care units; and 3) delirium (**Supplementary Table 2**, https://links.lww.com/CCM/H863). Searches were limited to English-language publications to ensure accurate interpretation of study content and narrowed to the publication date range from 2000 to the present. This date range was applied to ensure inclusion of studies employing standardized definitions and contemporaneous management practices for AKI and delirium, as earlier studies often used inconsistent criteria that would limit comparability. In addition to subscription databases, Google Scholar was used to supplement this search. Currently, there are no best practice guidelines that state how many Google Scholar results to review for systematic reviews (e.g., Cochrane Handbook, Joanna Briggs Institute). In fact, many systematic reviews opt not to search Google Scholar, but our team believe this was important to perform a supplemental Google Scholar search and 200 results seemed reasonable since Google results are based on relevancy ranking (29). Bibliographies from included studies were reviewed using the web-based tool Covidence (www.covidence.org) (Veritas Health Innovation Ltd., Melbourne, VIC, Australia).

Study Screening and Selection

Two reviewers (P.K., A.C.) independently screened study titles and abstracts, followed by full-text assessment to determine eligibility using Covidence. Any discrepancies were resolved through discussion. Eligible studies met all of the following criteria: 1) clinical trials or observational studies reporting individual patient-level data; 2) reported both AKI and delirium using validated definitions; 3) focused on a population admitted to ICU (**Supplementary Table 3**, https://links.lww.com/CCM/H863) (30); 4) published between January 2000 and January 2025; and 5) written in English. Studies were excluded if they were case reports, case series, or pre-clinical/experimental investigations.

Data Extraction

Two reviewers (P.K., A.C.) independently extracted data using Covidence, resolving any disagreements through discussion. Extracted data included study characteristics (design, setting, study period, and funding source); participant information (sample size, age, sex, ethnicity, primary diagnosis, comorbidities, and baseline kidney function); susceptibilities or exposures related to AKI and delirium (e.g., hypotension, toxins, sepsis, surgery, cognitive impairment, psychiatric illness, alcohol/substance misuse, sedation, analgesia, medications, and organ failures); and interventions (respiratory support, RRT, vasoactive agents, transfusions, nutritional support, extracorporeal life support, and surgical procedures).

The primary outcome was the proportion of critically ill patients with AKI who developed delirium, compared with those who did not. Secondary outcomes included: 1) the odds of critically ill patients with AKI, stratified by severity of AKI, who developed delirium compared with those who did not; 2) in-hospital mortality; and 3) health resource use, including the receipt and duration of organ support (mechanical ventilation [MV], RRT, vasopressors), length of ICU and hospital stay, and changes in baseline disposition among critically ill patients with AKI who developed delirium.

Quality Assessment

Two reviewers (P.K., A.C.) independently evaluated the risk of bias for all included studies, resolving any disagreements through discussion. The methodological quality of observational studies was assessed using the Newcastle-Ottawa Quality Assessment Scale (NOS) (31), including the following domains: study selection (representativeness of the exposed cohort, selection of the nonexposed cohort, ascertainment of exposure, and demonstration that outcome of interest was not present at start of study); comparability of cohorts; and outcomes (assessment of outcomes, follow-up, and adequacy of follow-up). Overall scores of 7–9 indicated high quality, scores of 4–6 represented moderate quality, and scores of 0–3 were considered low quality.

Data Analysis and Synthesis

Descriptive analyses were conducted for all included studies, summarizing study design, patient

characteristics, and susceptibilities/exposures. A meta-analysis was then performed to estimate the overall association between AKI and delirium. Furthermore, we examined clinical predictors and factors independently associated with delirium among critically ill patients with AKI, including AKI severity and receipt of organ supports. For dichotomous outcomes, results were summarized using pooled proportions, risk ratios (RRs), or odds ratios (ORs), while continuous outcomes were using weighted mean differences (WMDs), each with corresponding 95% CIs. Where data were reported as medians and interquartile ranges, they were converted to means and SDs using the mean-variance estimation method (32). Pooled meta-analyses were performed using a DerSimonian-Laird random-effects model to estimate overall effect sizes. Statistical heterogeneity was assessed through visual inspection of forest plots, the Q (χ^2) test, and the interclass correlation (I^2) statistic, with significant heterogeneity defined as I^2 greater than 50% or p value of less than 0.10 for the Q test. Publication bias was evaluated using funnel plots. All statistical analyses were two-sided, with a p value of less than 0.05 considered statistically significant, and were performed using STATA, Version 17 (StataCorp LLC, College Station, TX).

Certainty of Evidence

The Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach was used to assess the overall certainty of the evidence for each outcome, based on risk of bias, imprecision, indirectness, inconsistency, publication bias, large magnitude of an effect, dose-response gradient, and effect of plausible residual confounding.

RESULTS

Search Results

The initial search identified a total of 5343 citations, and after removing duplicates, 3778 unique results retrieved for title and abstract screening (**Fig. 1**). A further 3742 titles did not meet inclusion criteria, leaving 36 full-text articles to be assessed, of which, 18 studies were excluded, leaving a total of 18 publications fulfilling eligibility.

Study Quality

There were no randomized controlled studies, and the overall quality of the studies was moderate with mean NOS of 6.7 ± 1.3 and range of 4–8 (**Supplementary Fig. 1**, https://links.lww.com/CCM/H863). There were six studies (33.3%) rated as high quality, and 12 studies (66.7%) as a moderate quality; no studies were rated as poor quality.

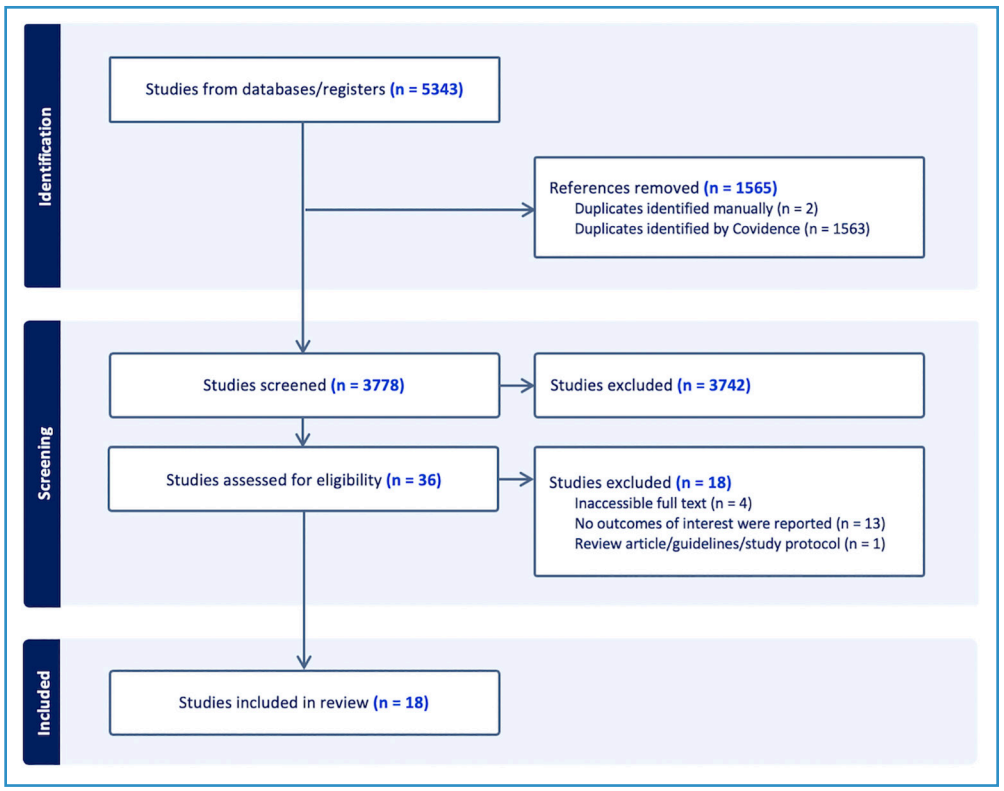

Figure 1. Preferred Reporting Items for Systematic Review and Meta-Analyses diagram.

Summary of Studies

All were observational studies comprising 158,694 critically ill patients (**Supplementary Table 4**, https://links.lww.com/CCM/H863). The population was mixed, including surgical ICU in ten studies, medical ICU in one, cardiac ICU in one, mixed ICU in five, and PICU in one. AKI was defined using the Kidney Disease: Improving Global Outcomes

criteria in eight studies, the AKI Network criteria in one, and without being clarified in nine (**Supplementary Table 5**, https://links.lww.com/CCM/H863). Delirium was assessed using the Confusion Assessment Method for the ICU in 12 studies, the Diagnostic and Statistical Manual of Mental Disorders (DSM)-4 in one, DSM-5 in one, the Nursing Delirium Screening Scale in one, the Cornell Assessment for Pediatric Delirium score in one, and without mention in two. The pooled proportion of delirium among patients with AKI was 32% (95% CI, 18–47; $p < 0.01$; $I^2 = 100\%$; **Fig. 2**).

Severity of AKI

In the stratified analysis by AKI stage, five studies, which included 3180 patients, reported the effect size of AKI stages 1 and 2 on the proportion of delirium, while six studies, which included 3872 patients, reported for AKI stage 3. Pooled unadjusted data using no AKI as a reference showed a stepwise increased in odds of delirium with more severe AKI stage: AKI stage 1 (OR, 1.68; 95% CI, 1.15–2.43; $p = 1.00$; $I^2 = 0\%$; low certainty; **Table 1**; and **Supplementary Fig. 2*A***, https://links.lww.com/CCM/H863), AKI stage 2 (OR, 2.13; 95% CI, 1.06–4.63; $p = 1.00$; $I^2 = 0\%$; low certainty; Table 1; and **Supplementary Fig. 2*B***, https://links.lww.com/CCM/H863), and AKI stage 3 (OR, 4.76; 95% CI, 2.27–12.29; $p = 0.75$; $I^2 = 0\%$; low certainty; Table 1; and **Supplementary Fig. 2*C***, https://links.lww.com/CCM/H863).

Type of Delirium

Two studies reported delirium subtypes among patients with and without AKI (Supplementary Table 5, https://links.lww.com/CCM/H863). Of 383 patients with AKI, 230 (60.1%) developed delirium, categorized as hyperactive (20.4%), hypoactive (34.3%), and mixed delirium (45.2%). Furthermore, the data suggested that AKI stages 2 and 3 were associated with all types of delirium, with an OR of 1.69 (95% CI, 1.04–2.73; $p = 0.03$) compared with AKI stage 1. One case-control study focused specifically on the hyperactive delirium subtype and reported an occurrence of 50% among patients with AKI, with risk increasing according to AKI severity: stage 1 (OR, 1.28; 95% CI, 0.70–2.34); stage 2 (OR, 1.44; 95% CI, 0.48–4.35); and stage 3 (OR, 5.40; 95% CI, 2.33–12.51). These findings indicated that AKI stage 3 was a significant risk for the development of hyperactive delirium.

Association With BUN

Three studies, including 1183 delirious and 3777 nondelirious patients, reported on the association between BUN and delirium (**Supplementary Fig. 3**, https://links.lww.com/CCM/H863). Higher BUN levels were significantly associated with delirium (WMD, 0.58 mg/dL; 95% CI, 0.37–0.78 mg/dL; $p < 0.01$; $I^2 = 29.25\%$).

Mortality

Ten studies, which included 1491 delirious and 2312 nondelirious patients, reported on in-hospital mortality among critically ill patients with AKI (**Fig. 3**). Pooled unadjusted analysis suggested that patients developing delirium had significant higher mortality (24.4% vs. 18.8% for delirium vs. nondelirium patients; RR, 2.36; 95% CI, 1.61–3.47; $p < 0.01$; $I^2 = 80\%$; moderate certainty), compared with patients with AKI not experiencing delirium (Table 1).

Renal Replacement Therapy

Seven studies, which included 2278 delirious and 5373 nondelirious patients, reported on receipt of RRT (**Fig. 4**). There was greater RRT use among patients with AKI who developed delirium compared with those not experiencing delirium (11.3% vs. 3.9% for delirium vs. nondelirium patients; RR, 3.12; 95% CI, 1.89–5.15; $p < 0.01$; $I^2 = 76\%$; moderate certainty; Table 1).

Mechanical Ventilation

Ten studies, which included 19,517 delirious and 136,291 nondelirious patients, reported on receipt of MV (**Supplementary Fig. 4**, https://links.lww.com/CCM/H863). There was greater MV use for those with delirium (2.6% vs. 0.5% for delirium vs. nondelirium patients; RR, 2.08; 95% CI, 1.46–2.98; $p < 0.01$; $I^2 = 99\%$; low certainty; and Table 1). In addition, eight studies, which included 2593 delirious and 3982 nondelirious patients, compared MV duration between groups and pooled analysis found no difference (WMD, 1.15 d; 95% CI, −0.07 to 2.38 d; $p < 0.01$; $I^2 = 99\%$; low certainty; Table 1; and **Supplementary Fig. 5**, https://links.lww.com/CCM/H863).

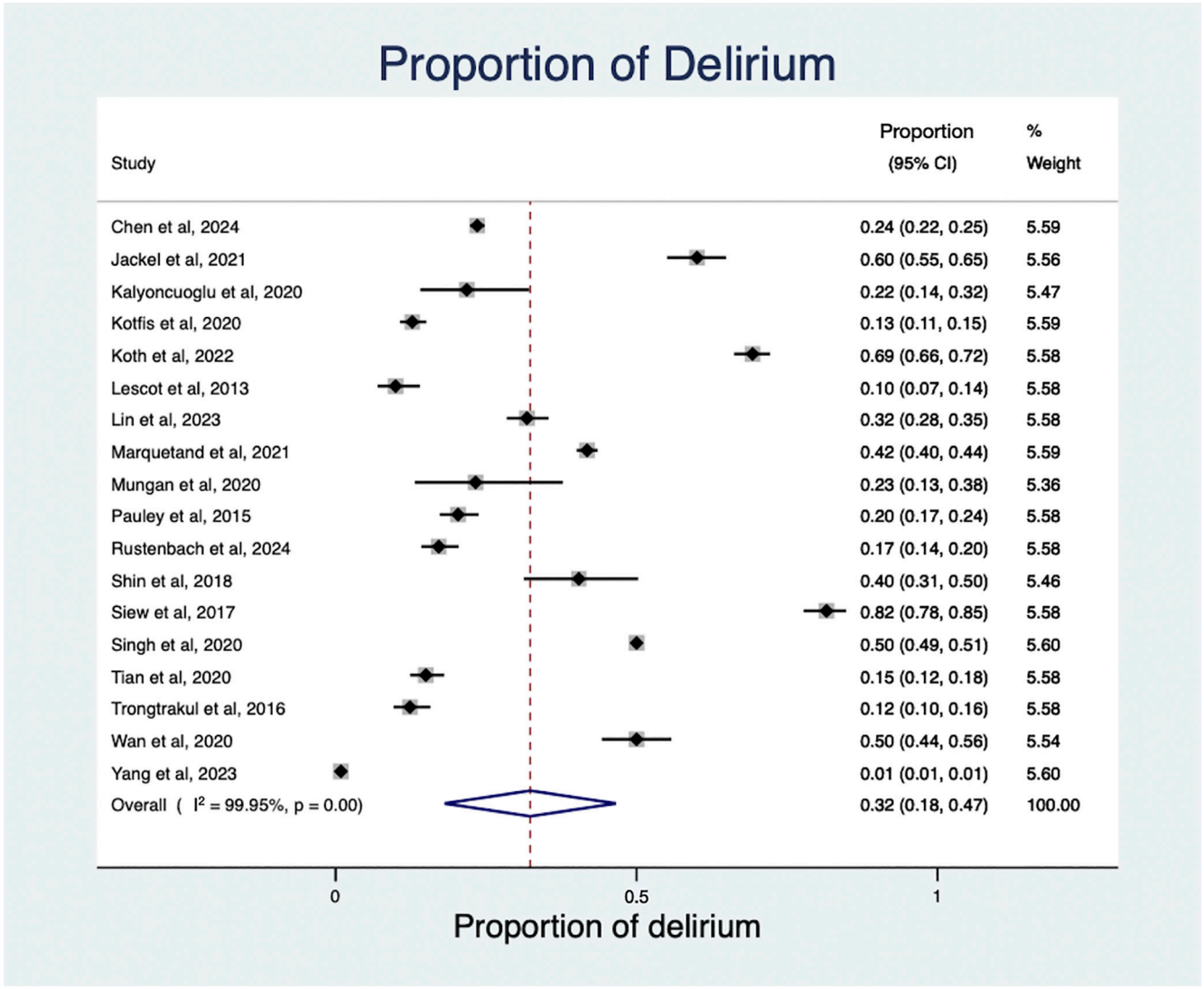

Figure 2. Proportion of delirium among critically ill patients with acute kidney injury in the included studies.

Vasopressors

Four studies, which included 1523 delirious and 4367 nondelirious patients, compared the use of vasoactive therapy between these groups (**Supplementary Fig. 6**, https://links.lww.com/CCM/H863). There was more vasopressor use among those with delirium (76.7% vs. 43.6% for delirium vs. nondelirium patients; RR, 1.61; 95% CI, 1.20–2.16; $p < 0.01$; $I^2 = 79\%$; low certainty; Table 1).

ICU and Hospital Length of Stay

Ten studies, which included 2802 delirious and 4126 nondelirious patients, reported on ICU length of stay (LOS; **Fig. 5*A***). There was longer ICU stay among those with delirium (WMD, 3.54 d; 95% CI, 1.20–5.87; $p < 0.01$; $I^2 = 99\%$; moderate certainty; and Table 1). In addition, another ten studies, which included 3,489 delirious and 117,691 nondelirious patients, reported on hospital LOS (**Fig. 5*B***). There was similarly longer hospital stay among those with delirium (WMD, 4.78 d; 95% CI, 3.48–6.09; $p < 0.01$; $I^2 = 91\%$; moderate certainty; Table 1).

Change in Baseline Disposition

Only one study reported on discharge disposition (Supplementary Table 5, https://links.lww.com/CCM/H863). The discharge destinations included home, skilled nursing facility (SNF), long-term acute care (LTAC), or other. As a result, the study reporting on

TABLE 1.
Grading of Recommendations, Assessment, Development, and Evaluation Summary of Findings for Outcomes in Acute Kidney Injury Patients With and Without Delirium the Included Studies

Outcomes	Relative Effect; Studies/Patients	Estimated Absolute Effect Size			Certainty of Evidence (Grading of Recommendations, Assessment, Development, and Evaluation)	Key Messages in Summary
		Delirium	No Delirium	Difference		
Mortality	RR, 2.36 (95% CI, 1.61–3.47); based on data from 3,803 patients in ten studies	271 per 1,000	97 per 1,000	174 per 1,000 (95% CI, 55–292 per 1,000)	⊕⊕⊕◯ Moderate[a]	AKI and delirium probably were associated with mortality
RRT	RR, 3.12 (95% CI, 1.89–5.15); based on data from 7,651 patients in seven studies	159 per 1,000	55 per 1,000	104 per 1,000 (95% CI, 24–184 per 1,000)	⊕⊕⊕◯ Moderate[a]	AKI and delirium probably were associated with receipt of RRT
ICU LOS	WMD, 3.54 d (95% CI, 1.20–5.87 d); based on data from 6,928 patients in ten studies	Mean, 8.30	Mean, 5.48	MD, 2.82 (95% CI, 1.75–5.85)	⊕⊕⊕◯ Moderate[a]	AKI and delirium probably were associated with prolonged length of ICU stay
Hospital LOS	WMD, 4.78 d (95% CI, 3.48–6.09 d); based on data from 121,180 patients in ten studies	Mean, 26.49	Mean, 24.30	MD, 2.19 (95% CI, −2.47 to 15.15)	⊕⊕⊕◯ Moderate[a]	AKI and delirium probably were associated with prolonged length of hospital stay
AKI 1	OR, 1.68 (95% CI, 1.15–2.43); based on data from 3,180 patients in five studies	N/A	N/A	N/A	⊕⊕◯◯ Low[b]	AKI stage 1 may be associated with incident delirium
AKI 2	OR, 2.13 (95% CI, 1.06–4.63); based on data from 3,180 patients in five studies	N/A	N/A	N/A	⊕⊕◯◯ Low[b]	AKI stage 2 may be associated with incident delirium
AKI 3	OR, 4.76 (95% CI, 2.27–12.29); based on data from 3,872 patients in six studies	N/A	N/A	N/A	⊕⊕◯◯ Low[b]	AKI stage 3 may be associated with incident delirium
MV	RR, 2.08 (95% CI, 1.46–2.98); based on data from 155,808 patients in ten studies	609 per 1,000	427 per 1,000	182 per 1,000 (95% CI, 141–223 per 1,000)	⊕⊕◯◯ Low[b]	AKI and delirium may be associated with receipt of MV

(*Continued*)

TABLE 1. (*Continued*)
Grading of Recommendations, Assessment, Development, and Evaluation Summary of Findings for Outcomes in Acute Kidney Injury Patients With and Without Delirium the Included Studies

Outcomes	Relative Effect; Studies/Patients	Estimated Absolute Effect Size			Certainty of Evidence (Grading of Recommendations, Assessment, Development, and Evaluation)	Key Messages in Summary
		Delirium	No Delirium	Difference		
Duration MV	WMD, 1.15 d (95% CI, −0.07 to 2.38 d); based on data from 6,575 patients in eight studies	Mean, 3.40	Mean, 2.16	MD, 1.24 (95% CI, 0.32–2.06)	⊕⊕◯◯ Low[b]	AKI and delirium may be associated with prolonged MV support
Vasopressors	RR, 1.61 (95% CI, 1.20–2.16); based on data from 5,890 patients in four studies	562 per 1,000	317 per 1,000	245 per 1,000 (95% CI, 145–347 per 1,000)	⊕⊕◯◯ Low[b]	AKI and delirium may be associated with receipt of vasopressors

AKI = acute kidney injury, LOS = length of stay, MD = mean difference, MV = mechanical ventilation, N/A = not applicable, OR = odds ratio, RR = relative risk, RRT = renal replacement therapy, WMD = weighted mean difference.
[a]Upgraded 1 level for large magnitude of effect, upgraded 1 level for effect of potential residual confounding factors, and downgraded 1 for serious inconsistency due to statistical heterogeneity.
[b]Upgraded 1 level for effect of potential residual confounding factors and downgraded 1 for serious inconsistency due to statistical heterogeneity.

120 delirium and 470 nondelirium patients of post-discharge from cardiac ICU, delirium patients were less likely to be discharged home (59% vs. 85%), while more likely to a SNF (26% vs. 11%), LTAC (11% vs. 3%), and other (4% vs. 2%).

Publication Bias

Publication bias was assessed visually using a funnel plot for mortality; there was no significant evidence of publication bias (p for Egger test = 0.088; **Supplementary Fig. 7**, https://links.lww.com/CCM/H863). However, we did not construct funnel plots to evaluate the publication bias for other outcomes because fewer than ten studies were available.

DISCUSSION

Summary of Key Findings

We conducted a comprehensive systematic literature search and performed both qualitative and quantitative syntheses to examine the association between AKI and delirium among critically ill patients. In this systematic review of 18 observational studies, delirium was found to be common, affecting approximately 32% of critically ill patients with AKI. This association suggests a stepwise increased risk of developing delirium with worsening AKI stage. Furthermore, delirium was associated with a greater risk of mortality, increased receipt of RRT, MV, and vasoactive therapy, as well as longer ICU and hospital stays.

Context With Respect to Prior Literature

AKI is common among hospitalized, critically ill patients and is a recognized risk factor for new-onset delirium, although the mechanisms underlying kidney-brain interaction remain incompletely understood. Understanding this relationship is crucial for early identification of high-risk patients and for guiding interventions to improve outcomes, as delirium is associated with long-term adverse consequences such as persistent cognitive impairment, increased healthcare utilization, and higher mortality.

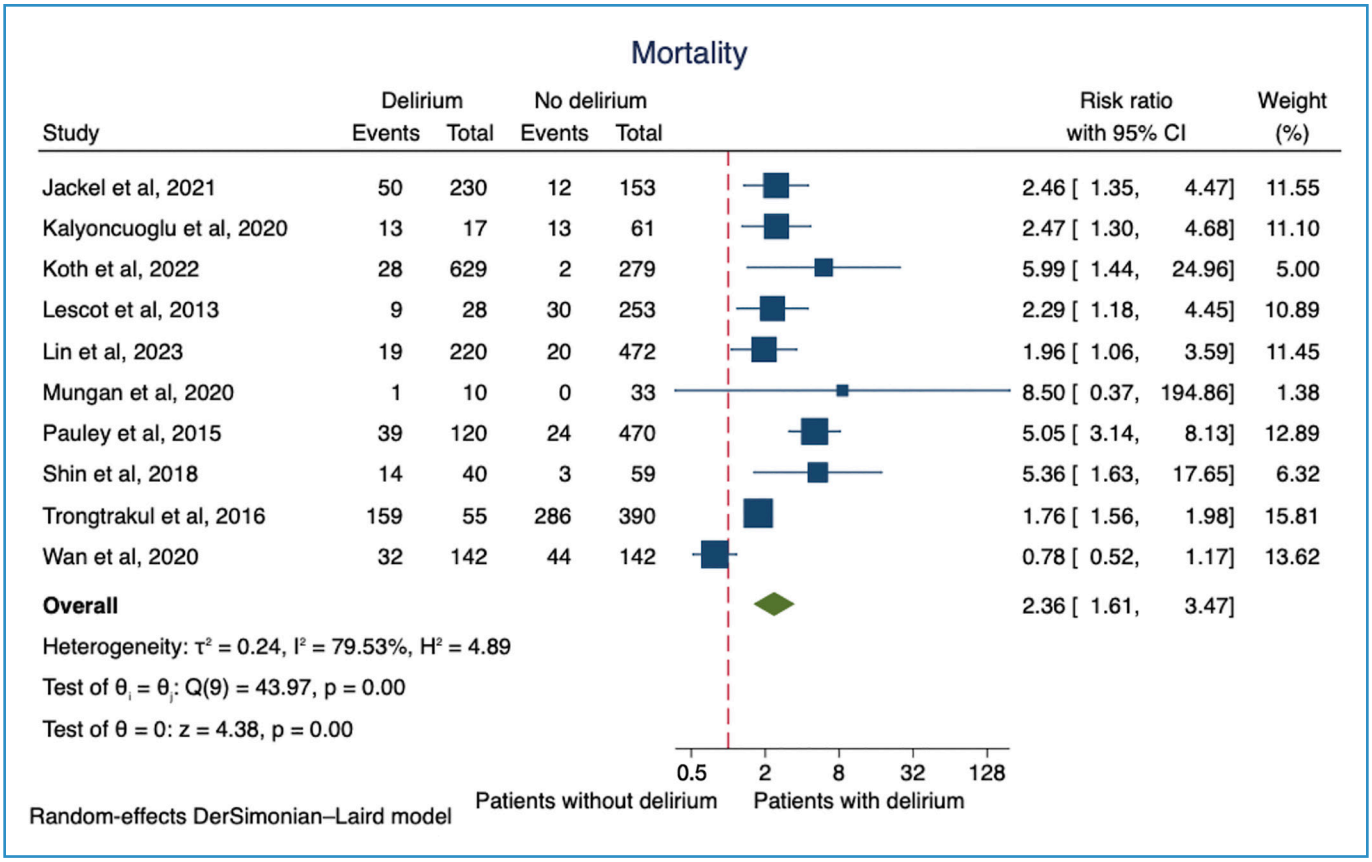

Figure 3. *Forest plot* of the risk ratio for mortality among critically ill patients with acute kidney injury who develop delirium and nondelirium.

Our findings are consistent with previous studies showing that AKI increases the risk of delirium, particularly in surgical populations, where factors such as intraoperative hemodynamic instability, anesthesia, sedatives, and perioperative analgesic use may contribute (17–21). The association likely involves systemic inflammatory pathways linking AKI to hippocampal injury and subsequent delirium (16). We also observed that delirium risk rises with AKI severity, plausibly due to heightened systemic inflammation, metabolic disturbances, and fluid-electrolyte imbalances.

Additionally, we explored the association between differences in BUN levels and the occurrence of delirium. We found that elevated BUN levels were associated with an increased risk of delirium. This may be explained by the accumulation of circulating BUN specifically or as a surrogate for any number of uremic toxins following AKI, which can result from increased production or impaired clearance. There is ongoing debate regarding whether BUN directly influences brain function. This uremic toxin and others may accumulate in various organs, including the brain, contributing to neurologic dysfunction and manifesting as delirium. Our findings support this hypothesis and suggest that interventions aimed at reducing circulating uremic toxins may potentially mitigate this neurologic consequence.

The combined burden of AKI and delirium contributes to worse clinical outcomes, including increased use of MV, vasopressors, and RRT, longer ICU and hospital stays, and higher mortality. Patients with delirium were also more likely to be discharged to nonhome destinations, although data on this outcome were limited. Most studies did not clarify the temporal or causal relationships among these factors, underscoring the need for future research to better define the directionality and mechanisms linking AKI, delirium, and health resource utilization.

Strengths and Limitations

This systematic review and meta-analysis provides a comprehensive synthesis of current evidence on the

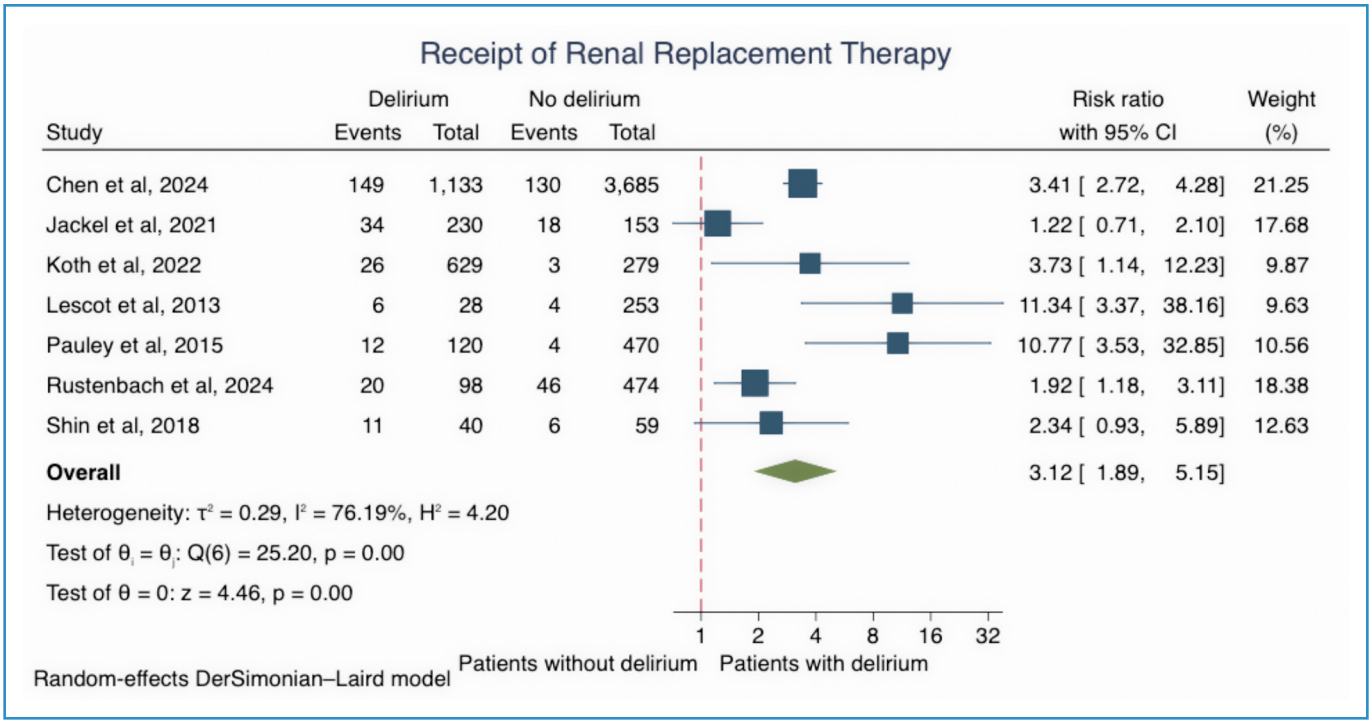

Figure 4. *Forest plot* of the risk ratio for receipt of renal replacement therapy among critically ill patients with acute kidney injury who develop delirium and nondelirium.

association between AKI and delirium in critically ill patients, examining occurrence, risk factors, outcomes, and healthcare utilization. Major strengths include a systematic and reproducible search strategy, prespecified analyses, assessment of publication bias, and application of the GRADE approach to evaluate the certainty of evidence.

However, several limitations should be acknowledged. The quality and heterogeneity of the included studies—varying in design, populations, delirium definitions, and outcome reporting—limit the robustness of pooled estimates. None of the studies used the gold standard for delirium diagnosis, and the timing of delirium onset relative to AKI was often unclear, restricting causal interpretation (33). Most studies were observational and retrospective, introducing potential bias and confounding. Furthermore, our analysis focused on delirium in patients with and without AKI, without assessing the reverse relationship—that is, the occurrence of AKI among patients with and without delirium. In addition, all studies included only ICU-admitted patients, with no data on those denied ICU admission or on long-term outcomes. Variability in the clinical recognition and documentation of AKI and delirium may also have influenced results. Limited availability of adjusted estimates and the need to convert or approximate some data for meta-analysis could have introduced imprecision.

Implications for Healthcare Providers, Policy, and Future Research

This review highlights key knowledge gaps and opportunities to improve ICU care for patients with both AKI and delirium. Early detection and management of AKI may help prevent delirium and reduce harmful kidney-brain interactions. Preventive measures include avoiding nephrotoxic and deliriogenic drugs, timely initiation of RRT, prompt administration of antibiotics and fluids, early weaning from MV, and ensuring adequate nutritional support.

Greater clinical awareness of delirium as an early warning sign of physiologic instability is essential. Routine delirium screening—especially at ICU admission—together with regular medication reviews and adherence to best practice prevention protocols, should be integrated into critical care practice. Continued research is needed to refine prevention and management strategies, improve patient outcomes, and inform health system resource planning for this high-risk population.

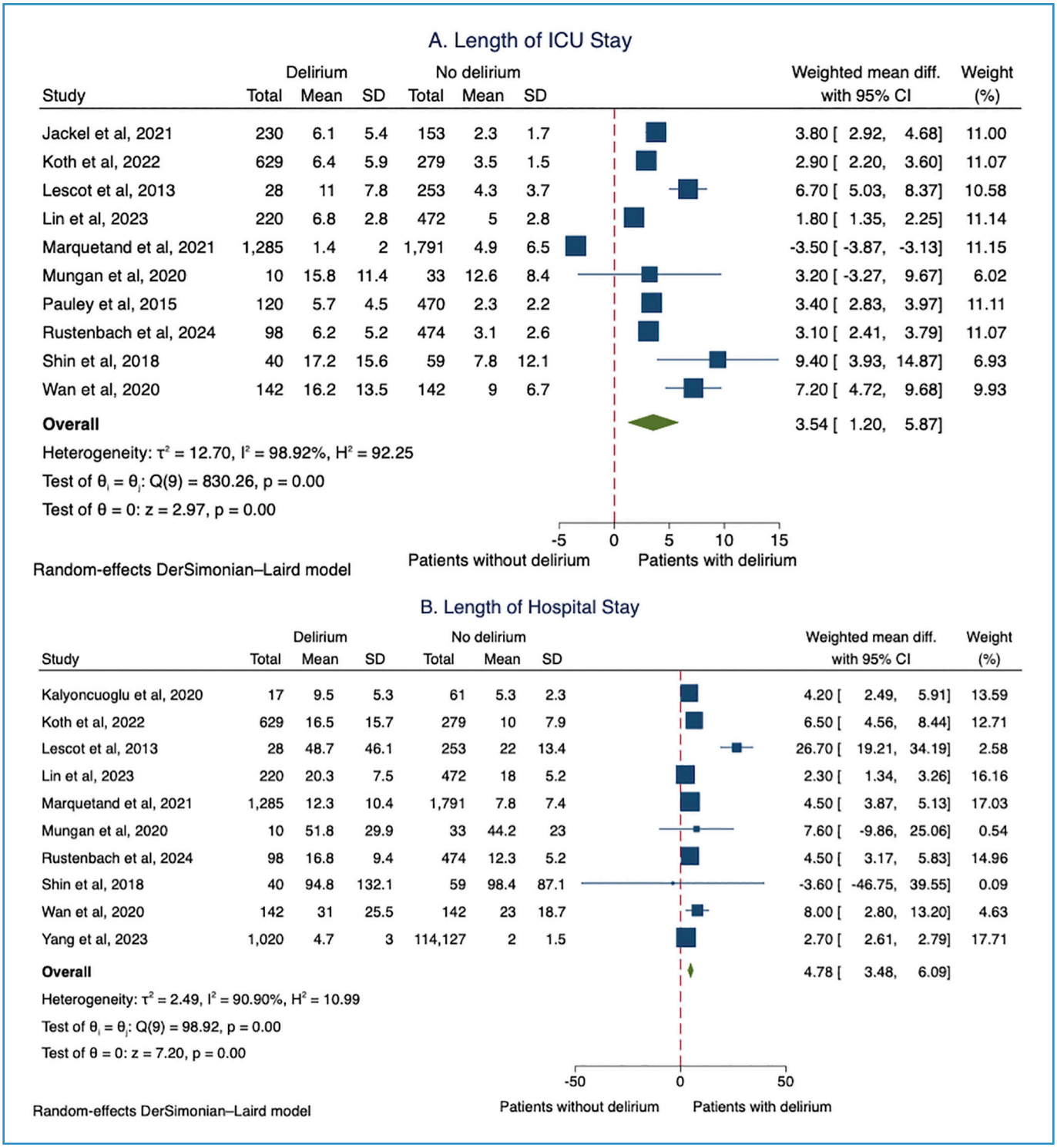

Figure 5. *Forest plot* of the weighted mean difference for length of stay (LOS) among critically ill patients with acute kidney injury (AKI) who develop delirium and nondelirium. **A**, ICU LOS. **B**, Hospital LOS.

CONCLUSIONS

Delirium is common among critically ill patients with AKI and is associated with worse clinical outcomes and greater health resource utilization. Strategies to improve recognition, monitoring, and mitigation of delirium in high-risk patients with AKI represent opportunities to potentially improve outcomes.

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Dr. Kusirisin was responsible for preparing the article. Dr. Kusirisin, Ms. Kung, Dr. Wilcox, and Dr. Bagshaw designed the study protocol. Ms. Kung refined the search strategy. Dr. Kusirisin and Ms. Corsaro screened, selected, extracted data, and assessed the quality of studies. Dr. Kusirisin performed qualitative and quantitative synthesis. Dr. Kusirisin, Ms. Corsaro, Dr. Rewa, Dr. Wilcox, and Dr. Bagshaw discussed and drafted the article. Dr. Bagshaw conceived the study and supervised the project. All authors reviewed and approved the final version of the article.

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